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Breast cancer-associated risk factors and management among women attending Medical Imaging departments' in Namibia.

By

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Thesis submitted in partial fulfilment of the requirements for the degree of master health sciences in the faculty of health and applied sciences.

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November 2021

DECLARATION

I, Martinlina Seranline Karutjaiva hereby declare that the work contained in the thesis entitled Breast cancer-associated risk factors and management among women attending Medical Imaging departments' in Namibia is my own original work and that I have not previously in its entirety or in part submitted it at any university or other higher education institution for the award of a degree.

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DEDICATION

This thesis is devoted to "**Women**" my mothers, my sisters, my daughters, my nieces, my aunts and my cousins. This one is for you. Your body is your temple your vessel and so still it is yours a given gift, you are fearfully and wonderfully made, oh beautiful woman. You are not defined by your circumstances nor by your situation. You are already beautiful because you are a "**Woman**". You are and will always be needed to be here!

By: "Tina Karutjaiva"

FOR I AM CONVINCED! Neither death nor life, neither angels nor demons, neither our fears for today nor our worries about tomorrow—not even the powers of hell can discrete us from God's love. [39] No power in the sky above or in the earth below—indeed, nothing in all creation will ever be able to discrete us from the love of God that is revealed in Christ Jesus our Lord.

ROMANS 8:3

ABSTRACT

Background: Breast cancer, a universal health trepidation, is the principal cause of death for women in Namibia. Observing patients with low calculated risk factors being diagnosed with breast cancer compel us to probe into the possible lifetime adopted risk factors compatibility and supervision of breast cancer in Namibia. Knowing and understanding risk factors for breast cancer may pave the way for better risks assessment and provide timely, accurate diagnostics, management and treatment strategies. Therefore, it is vital to determine and establish specific risk factors guidelines based on rigorous medical and demographic mapping for appropriate breast cancer screening methods, approve accurate patient diagnosis, and enhance the management of breast cancer in Namibia.

Purpose: This study assessed the most common breast cancer risk factors amongst Namibian women attending Medical Imaging. In addition, the study assessed the compatibility of the breast cancer risk pre-screening evaluation tool, specifically the Tyrer Cuzick model. Finally, the study assessed the management and treatment measures of breast cancer.

Methods: Phase 1 of this study was a mixed method of both prospective and retrospective cohort; breast cancer risk data was collected from 200 patients at Medical imaging and Ab May Oncology Centre, Namibia. The breast cancer risk factors data collected was used to evaluate the compatibility of the Tyrer Cuzick tool with Namibian women. Phase 2 of this study was a prospective study that sought the association of the diagnostic outcomes and recommendations concerning the management of breast disease using closed-ended and rating scale questions from 6 Oncologists at the AB May oncology centre in Windhoek.

Results: The results indicated that there is an association between women height and prevalence of breast cancer amongst Namibian women. Women between the ages of 40 to 65 are at high risk. Women detected with breast cancer who have knowledge of family history of breast were significantly low (13%) compared to participants of the control group of unknown family history of breast (28%) amongst those diagnosed with breast cancer. The use of HRT is uncommon among the case (2%) and the control (7%) groups participants respectively. 54% of the women detected with breast cancer had reached menopause. The average woman diagnosed with breast cancer was overweight, which was not significantly

different from the control group. Age at menarche was insignificantly but considerably late for the average Namibian women amongst the sample group at age 15. The average woman diagnosed with breast cancer Age at first pregnancy was 21. BIRADS category risk factor prediction was 88% with an 8.5% abnormal interpretation. The Tyrer Cuzick risk assessment tool was not compatible for risk assessment for this study; the average woman diagnosed with breast cancer had a low lifetime risk of 6-10% being the most the average case group mean was lower than the control group, both being low with 8.8% and 11.1% respectively. The most common type of breast cancer is invasive ductal carcinoma at 43%. The results also indicated that there is no genetic testing available regarding the treatment and management of breast cancer. The screening modalities are limited in the public sector, although patients still have access to various treatment methods, however, with limited resources.

Conclusion: Based on this study's results, height and Age are the most common and valid breast cancer risk factors. Although there are internationally established risk factors for breast cancer, the study suggests continuous research on breast cancer risk factors to create a specific range for different sectors. In addition, the BI-RADS category indicates to be a valid risk factor considered for follow-up visits for breast cancer screening. Other breast cancer risk evaluators considered or explored for Namibian women. Financial and educational support on screening modalities is needed for the treatment and management of breast cancer, especially at the state diagnostic and treatment centres to accommodate lower social-economic groups.

GLOSSARY

ALND	Axillary lymph node dissection
BC	Breast cancer
BCT	Breast-conserving therapy
BI-RADS	Breast Imaging Reporting and Database System score
BRCA1/2	Breast cancer gene 1/2
BSE	Breast self-examination
CAD	Computer-aided detection
CC	Cranio-caudal view.
CHRT	Combined hormone replacement therapy
DCIS	Ductal carcinoma in situ
eGFR	Estimated glomerular filtration rate (eGFR is a number grounded on your blood test for creatinine, a waste produce in your blood. It tells how well your kidneys are working
FDA	Food and Drug Administration
FNS	Fine needle sampling
HBOC	Hereditary Breast and Ovarian Cancer Syndrome. It is considered when there are several cases of breast cancer and/or ovarian cancer on the same side of the family.
HIMS	Hospital information management system
HRT	Hormone replacement therapy
IARC	International Agency for Research on Cancer
IBC	Inflammatory breast cancer
IBTR	Invasive breast tumour recurrence
IDC	Invasive ductal carcinoma or infiltrating ductal carcinoma
ILC	Invasive lobular carcinoma

LABC	Locally advanced breast cancer
LMIC	Low and or middle-income countries
MPA	Medroxyprogesterone acetate
PET	Positron emission tomography. This test is sometimes used in breast cancer treatment.
SLNB	Sentinel lymph node biopsy
TNBC	Triple-negative breast cancer
VAB	Vacuum-assisted biopsy

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CHAPTER ONE

INTRODUCTION

1.1 Introduction

Breast cancer, a universal health alarm, is the principal cause of death for women in Namibia (Cancer Association of Namibia, 2017). Knowing and understanding risk factors for breast cancer pave the way for better risks assessment to provide timely, accurate diagnostics, management and treatment strategies. Risk assessment is necessary to establish whether a woman has an average or elevated risk for breast cancer and will also provide guidance on breast cancer surveillance, risk reduction, and genetic testing. Breast cancer risk assessment can also help patients and health practitioners to decide on preventative steps to lower the chances of breast cancer. The aetiology of breast cancer is far from being fully understood in developing countries. In countries with limited resources, breast cancer is usually distinguished in the progressive stages because early detection, diagnosis, and treatment are not promotable despite the overall breakthroughs in medicine (Rivera-Franco, 2018).

Breast cancer is the predominant leading cancer with 27.3% amongst Namibian women. Breast cancer diagnoses have increased from 309 per year from 2010 to 516 in 2017 (Namibian National Cancer Registry, 2017). Furthermore, the most common risk factors adopted are not specific to Namibian women. Establishing specific risk factors guidelines based on rigorous medical and demographic mapping may play a huge role in determining the correct route for managing the disease specificity regarding Namibian women. Since establishing the Medical Imaging Departments for breast screening in Windhoek, analysis and interpretation of common risk factors of breast cancer have also seemingly increased. Research on the causes of breast cancer has progressed to the stage where we can define the profile of females at high risk for the disease with some certainty (National Breast and Ovarian Cancer Centre, 2009). Certain factors called “risk factors” raises the likelihood of women developing breast cancer (Lakshmi, Athira, Mary & Vijayalakshmi, 2012). Which also seems to increase the lifetime risk calculations during risk assessment for breast cancer. The Tyrer-Cuzick tool calculates the lifetime risk for breast cancer using the clinical setting patient breast cancer risk data. However, patients with low calculated risk are being diagnosed with breast cancer. It is essential that tools used to calculate the possible lifetime risks be compatible or adopted or established from rigorous medical and demographic mapping acquired from the patient data to a certain degree.

The population used for this research were women above 18 with and without breast cancer who went for breast screening, follow up, treatment and breast disease diagnoses. The goal was to analyse the results corresponding to the outcomes from the earliest visit to the Imaging Department and consider records and reports from Medical Imaging and AB May oncology departments.

1.2 Background information

Breast cancer in developing countries is familiarized as a significant public health problem; there is, however, minimal evidence of its epidemiology and management in the Southern parts of Africa (Balekouzou et al., 2016). The amplified incidence of breast cancer in a group of women active in social and professional life observed in the Namibian National Cancer Registry (NNCR) from 2010 to 2017 implies the need for multidirectional research to identify risk factors associated with this type of neoplasm. This study aims to identify the most common breast cancer risk factors and determine the compatibility of the Tyrer Cuzick risk assessment evaluator to assess different management methods of breast cancer for Namibian women. Assessing the common risk factors and the management of breast cancer might help in determining which management methods are seemingly best linked to the type of breast disease or if the management methods according to the patient diagnosis and management of the disease are compatible based on the outcome of the disease up to the year 2020.

1.3 Research problem statement

It is observed that Namibia does not seem to have a specific range for the most common risk factors specific to Namibian women, and this may play a huge role in determining the correct route for managing the disease-specific to Namibian women, which might play a role in the prevention and cure of the disease. The research was encouraged by the Namibian National Cancer association, which according to the Namibian National Cancer registry, aims to “use observed cancer trends to predict future cancer patterns in Namibia and to provide information on the burden of cancer in different regions and among different ethnic groups in Namibia” (NNCR, 2017). The second reason for conducting this research is due to curious observation made by the researcher as a Radiographer at Medical Imaging that according to the Tyrer-Cuzick assessment tool used at the Imaging Departments, not all women with a high risk for breast cancer seemingly have BIRADS 3 and above or according to the patient’s reports have any suggestive concern of breast cancer. The Namibian Cancer Association further encourages that the Namibian cancer registry is used as a guide to investigating risk factors for the principal cancers in Namibia amongst

women, breast cancer (NNCR, 2017). Significant increase in the overall incidence of cancer in both males and females in Namibia (excluding non-melanoma skin cancers) from 100.7 per 100 000 to 144.2 for 100 000 males and from 90.2 per 100 000 to 138.7 per 100 000 females from the preceding reporting period should be cautiously investigated (NNCR, 2017).

Adopting tools or assessment methods for breast cancer risk factors that may not be on local medical and demographic mapping might produce different outcomes. Assessing the common risk factors, the management of breast cancer, and the prevalence of the disease might help determine the appropriate breast cancer screening methods, approve accurate patient diagnosis, and enhance the management of breast cancer in Namibia.

1.4 Research Aim and Specific objectives

1.4.1 Research Aim

This research aims to assess the most common risk factors of breast cancer amongst Namibian women visiting the Medical Imaging departments to determine whether the breast cancer pre-screening tool used to consider the risk factors assessed is compatible for Namibian women. Finally, the study assesses the management and treatment procedures of breast cancer in Namibia.

1.4.2 Research Objectives

1. To assess the most common risk factors of breast cancers among Namibian women visiting the Medical Imaging departments.
2. To assess and contrast the screening modalities at the Medical Imaging departments with specific reference to the Tyrer-Cuzick tool.
3. To assess the breast cancer management and treatment procedures in Namibia

1.4.3 Research Questions

This study pursues to respond to the following research questions:

- What are the most common risk factors associated with women that have been diagnosed with breast cancer in Namibia?
- Is the risk assessment tool used currently correlated with the diagnostic outcome of the Tyrer- Cuzick model for breast cancer risk assessment?
- What amendments can consider elevating ordinary management regimens for breast cancer patients attending the Medical Imaging departments in Namibia?
- Which are the common risk factors influencing breast cancer to establish a risk factor reference range specific to Namibian women?

- Which are the most common types of breast cancer and methods used to fight breast cancer after the diagnosis?

CHAPTER TWO

LITERATURE REVIEW

2.1 Breast Cancer Aetiology

2.1.1 Breast Cancer

Breast cancer is a molecularly diverse illness, which is categorised by high genomic uncertainty demonstrated by somatic gene mutations, copy number modifications, and chromosome structural movements (Testa, CastelliP & Pelosi, 2020). Breast cancer commences when breast cells start increasing out of control. Usually these cells form a tumour that can be seen on x-ray or a lump that can be felt by touch. The tumour is malignant when the cells metastasize to a remote area of the body. Breast cancer occurs mostly in women and has been observed in men (American Cancer Association, 2018), with 70 to 80 % of patients with early-stage, non-metastatic illness which can be cured however, advanced breast cancer with remote organ metastases is considered incurable with current treatments (American Cancer Association, 2018).

Generally, cancer develops when the immune system does not function properly or when the number of cells produced is vast to be eliminated (Sharma, Dave, Sanadya, Sharma & Sharma, 2010). Breast tumours naturally begin with ductal hyperproliferation developing into benign tumours or even metastatic carcinomas following stimulation by multiple carcinogenic variables such as environmental factors, type of food consumption and exposure to radiation (Sun et al., 2017).

Breast cancer may start in several places in the breast. Most breast cancers start in the milk ducts that lead to the nipple (ductal cancers). Some of them start in the glands that create milk in the breast (lobular cancers) A small percentage of breast cancers begin in other breast tissue such as sarcomas and lymphomas; these tumours may not be breast cancers. Although numerous forms of breast cancer can cause a lump in the breast, not all of them do (American Cancer Society, 2019).

Breast cancer is a disease with a broad variety of histological and biological characteristics, clinical presentations which requires a unique therapeutic attitude and response.

2.1.2 Types of breast cancer

2.1.2.1 Ductal Carcinoma in Situ (DCIS)

About 1 in 5 new breast cancers are ductal carcinoma in situ (Fu et al., 2018). Almost all women with breast cancer in this stage can be cured. Intraductal carcinoma, or stage 0 breast cancer, is alternative name for DCIS. DCIS is a type of breast cancer that is non-invasive or pre-invasive. This shows that the cells that line the ducts have transformed into cancer cells, but they have not moved beyond the duct walls into the neighbouring breast tissue(Gupta & Garg, 2020). Because DCIS has not spread to the surrounding breast tissue, it cannot spread (metastasize) outside the breast to other parts of the body. However, DCIS can occasionally turn into invasive cancer. By then, the cancer has spread from the duct to adjacent tissue and could metastasize to other parts of the body from there. By then there is no good way to be sure which one will, and which will not develop into invasive cancer, which is why almost all women are treated with DCIS (American Cancer Society, 2021).

2.1.2.2 Invasive ductal carcinoma (IDC)

Breast cancer histology accounts for up to 25% of all invasive cancers (Weigelt, Geyer & Reis-Filho, 2010). The utmost common form of breast cancer is invasive ductal carcinoma(Society, 2016). The breast ducts are referred to as 'ductal.' milk directed to the nipple via these tubes. As cells in the ducts begin to divide and grow abnormally, this is how breast cancer starts. The word "invasive" refers to cancer cells that have spread outside the ducts to adjacent breast tissue. Breast cancer ‘’of no specific type’' or ‘’not otherwise defined’' is a term used to describe invasive ductal breast cancer. This is based claiming the malignancy cells have no highlights that class them as a sort of breast disease when analysed under the microscope. Sometimes invasive ductal breast cancer is found blended with other sorts of breast cancer within the breast (Breast Cancer Now, 2020). Shown below are Figure 2.1 and Figure 2.2 presenting mammography and breast ultrasound images respectively of a 40-year-old female with no breast disease symptoms, diagnosed with right breast IDC. Figure 2.1 “A” shows the right breast cranial caudal (CC) view and Figure 2.1 “B” shows the right breast mediolateral oblique (MLO) view.

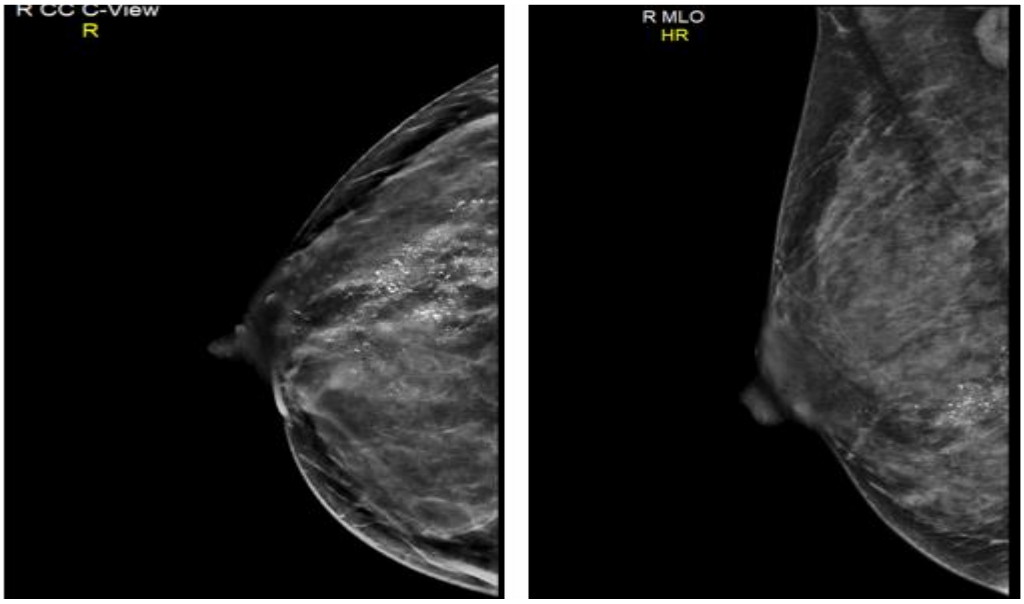


Figure 2.1: A large group of segmental malignant pleomorphic micro calcification is seen within th A ral breast of the right breast. B iagnosis of this patient was micro-invasive ductal carcinoma in situ

(Medical Imaging, 2020)

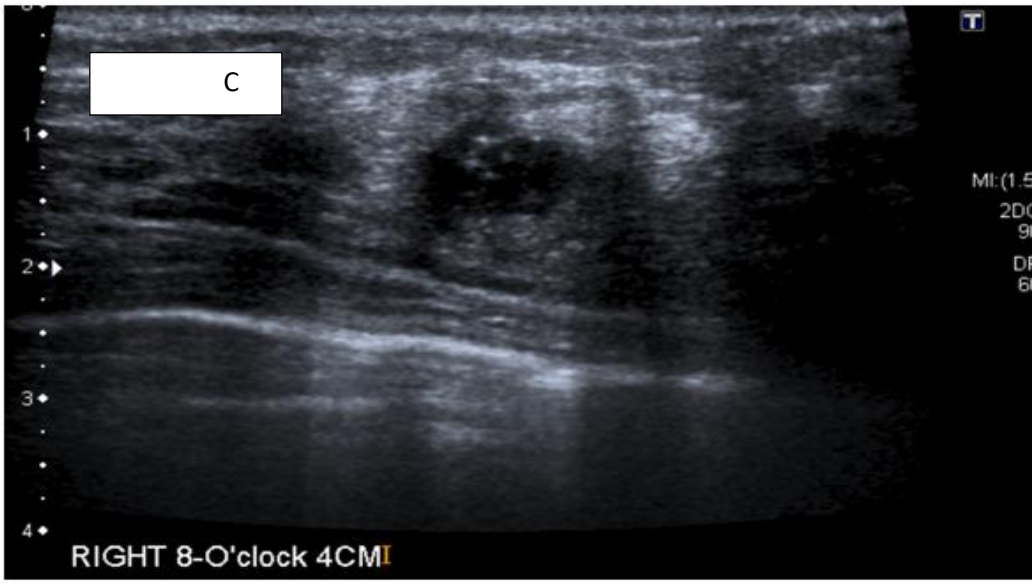


Figure 2.2: Ultrasound revealing multiple areas of ill-defined mixed hypo-and hyper echoic changes within the right breast, most pronounced in the 8:00 position

(Medical Imaging, 2020)

2.1.2.3 Invasive breast cancer (ILC or IDC)

Invasive (or infiltrative) breast cancer has spread to the neighbouring breast tissue. The utmost common types are invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC). Invasive ductal carcinoma accounts for about 70-80% of all breast cancers (American Cancer Society, 2021). The most common morphological subtype of breast cancer is invasive lobular carcinoma, accounting for up to 15% of all cases. Such tumours usually have a lower tissue grade and reduced mitotic index, hormone receptor positive and HER2, p53 genes, and basal marker negative, and a normally good response to endocrine therapy with a good prognostic phenotype. Despite this, physicians face many difficulties in diagnosing and treating patients, as it is difficult to detect such cancers by screening, it elicits an invasive nature and a proclivity for metastatic colonization on a broad scale, and as a consequence, a worse long-term unfavourable outcome when compared to invasive carcinoma of any kind (Reed, 2015).

2.1.2.4 Paget's disease of the nipple

Sir Paget first identified Paget's disease in 1874 as an eczematous nipple lesion associated with an underlying cancer. Paget's disease of the breast is a cancerous disorder that manifests as an eroding and bleeding nipple ulcer. Paget's disease is a rare breast cancer, representing 1–3% of all breast cancers in women and in 1.4 to 13% of cases. It occurs as an isolated affection, and in 90–100% of cases, it is associated with an in situ or invasive glandular carcinoma. In about a third of the cases, in situ histology is discovered. The average age at which the disease presents itself is at 56 years. A mammogram is performed whenever Paget's disease is suspected, to identify micro calcifications that are heterogeneous, poorly limited, and have suspicious opacities. Mammary echography is conducted in a systematic manner to classify formations that attenuate ultrasound and assist biopsy. To determine whether there is an underlying cancer, additional specialized images can be used such as Magnetic Resonance Imaging (MRI). The prognosis depends on the underlying breast cancer. The treatment recommendations are limited, which include conservative surgery, or a mastectomy based on a patients' age (Dubar et al., 2017).

2.1.2.5 Phyllodes tumours of the breast

Phyllodes tumour is a very rare breast tumour, which accounts for just 0.3 to 0.9 percent of all breast tumours. There are three types of phyllodes tumours: benign, borderline, and malignant. They are most common in women among the ages of 40 and 50. However in a study done by Ditsatham and Chongruksut the average age of diagnosis was early as 35 years. A painless and, swiftly rising mass is the most common clinical appearance. If the tumour is a well-circumscribed oval or lobulated mass with rounded borders, images from mammography and ultrasonography showed suspect phyllodes tumour, that have a lobulated shaped mass. Most imaging features make it difficult to tell the difference between fibroadenoma and phyllodes tumour, therefore tumour's scales should be considered. Fibroadenomas are usually 2 cm in diameter, while phyllodes tumours are 4 to 7 cm in diameter. Surgical removal with a margin of at least 1 cm is the recommended treatment for phyllodes to minimize the rate of recurrence (Ditsatham & Chongruksut, 2019). Figure 2.3 shows four mammographic images of a patient with a right breast phyllodes tumour, in two different views right MLO view "A" on the top and right breast CC view at the bottom Image "C".

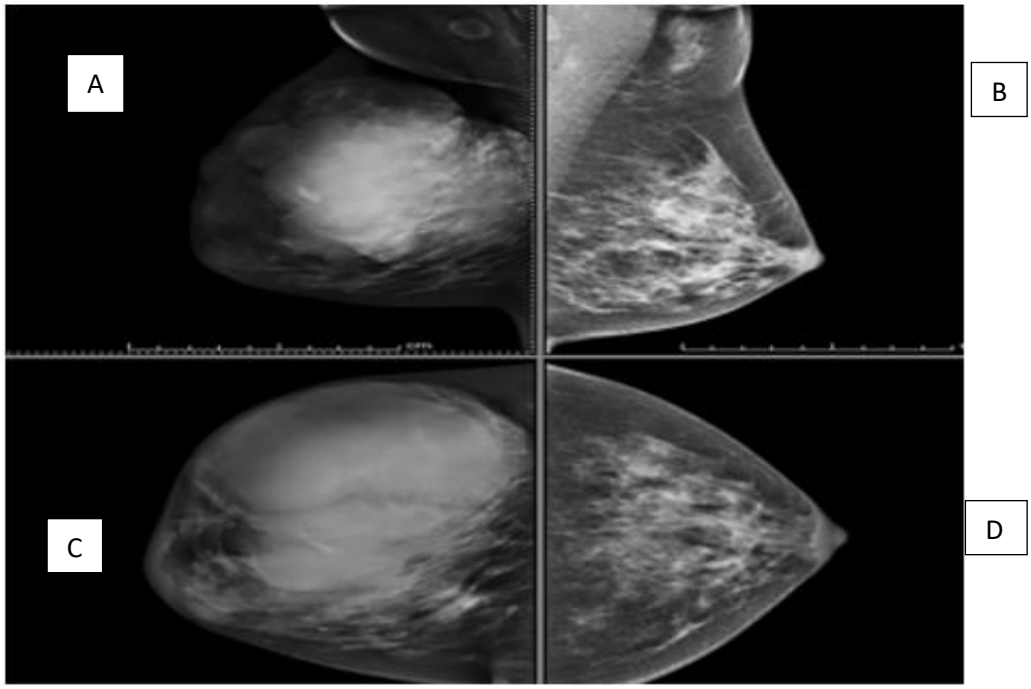


Figure 2.3: Female breast presenting phyllodes tumour on mammogram right breast. The four images demonstrate mammography images of a patient's breast with large lobulated tumour with the diagnoses of phyllodes tumour of the right breast images "A"

MLO view and “C” CC view. The left breast is showed in comparison to the right “B” MLO view and “D” CC view of the left breast of the same patient (Ditsatham and Chongruksut, 2019). Printed with permission.

2.1.2.6 Locally advanced breast cancer (LABC)

The term locally progressed breast cancer (LABC) is used to define breast cancer that is locally advanced but has not yet spread outside of the breast and local lymph nodes. The LABC has variety of clinical and biological characteristics. In developing countries, LABC is a very common clinical presentation of mammary carcinoma that accounts for 30 to 60% breast carcinomas (Gedam, Shukla & Ingale, 2018). Locally advanced breast cancer also refers to patients diagnosed with massive primary cancers and / or regional adenopathy. Its incidence has drastically decreased due to mammographic screening and early detection. However, due to the high risk of being diagnosed with locally advanced disease, patients remain to experience a unreasonably high death rate from breast cancer (Newman, 2009). In most cases LABC is palpable and visible on x-ray. For patients, diagnosed with LABC, multidisciplinary therapy has become the treatment of choice (Gedam et al., 2018).

2.1.2.7 Metastatic breast cancer

Breast cancer most commonly spreads to the brain, bones, and liver through a series of events including: (1) local invasion and migration across the epithelial basement membrane and the stroma's connective tissue; (2) intravasation into blood or lymphatic vessels to enable diffusion; and (3) extravasation and permeation into tissue parenchyma, followed by eventual colonization of secondary organ sites (Schiemann, 2020). Since details from a patient's primary tumour may not precisely represent the metastasis, the unpredictability of metastatic tumours remains a significant barrier to personalize (Marino et al., 2013). Metastatic breast cancer is also termed stage IV (4) breast cancer. Although cancer is in different parts of the body and a patient had a mastectomy, this physiological state usually also corresponds best breast cancer treatments and no other treatment methods (Cancer Support Community, 2021). Figure 2.4 shows the spread of breast cancer, which mostly occurs in the brain, lungs, liver and the bones.

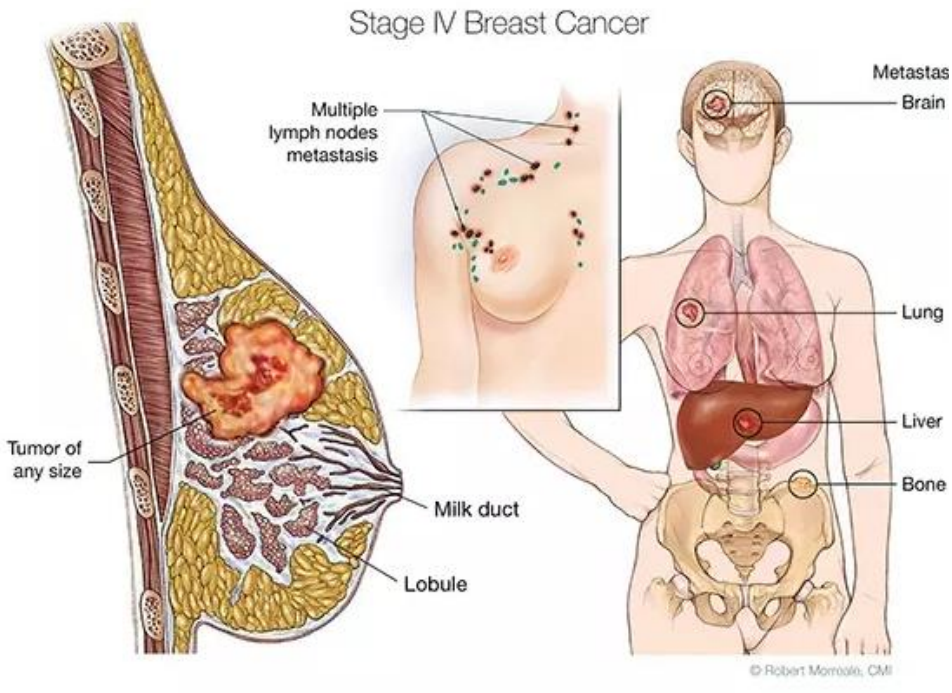


Figure 2.4: Metastatic breast cancer spread around different organs of the body; brain, lung, liver and bone with multiple lymph nodes metastasized (Cancer Support Community, 2021).

2.1.3 Breast cancer Genes

Several genes cause alterations and irregular intensification of both oncogenes and anti-oncogenes roles in tumour initiation and growth. The risk ratio of breast cancer in women older than 70 years with BRCA1 (breast cancer gene 1) or BRCA2 (breast cancer gene 2) mutations was 57 % and 49%, respectively (Chen in 2007). Both genes code for tumour suppressor proteins, cell cycle checkpoint dysregulation, abnormal centrosome replication, genetic variability, and apoptosis, all related to BRCA1 deficiency. The BRCA2 protein controls recombinational reparation in DNA double-strand breaks by interacting with RAD51 and DMC1. If a person inherits deleterious mutations in the BRCA1 or BRCA2 genes, such person's risk of breast cancer may be significantly increased (Sun et al., 2017).

2.1.3.1 C-erbB-2

A major oncogene in breast cancer, HER2 (human epidermal growth factor receptor 2), also identified as c-erbB-2, is found on the long arm of the human body chromosome

seventeen (17q12). HER2 over-expression, which is in around 20% of the primary breast cancers, through PTEN/Akt /mTORC1 signalling also the number of cancer stem cells and show poor clinical outcomes (Elizalde et al., 2016).

Tumour cell proliferation, advancement, and survival aid by changes in multiple cell signalling pathways. For example, the PI3K/Akt/mTOR pathway involves growth, proliferation, survival, motility, metabolism, and immune response control. One of the leading causes of cancer cell resistance to antitumor therapy is the activation of this pathway. This pathway may serve as a possible therapeutic target and a predictive and diagnostic tool (Elizalde et al., 2016).

2.1.3.2 Epidermal Growth Factor Receptor (EGFR)

EGFR, also referred to in humans as c-erbB-1 or Her1, is located on the short arm of chromosome 7; this helps to encourage cell proliferation, cell invasion, angiogenesis and to protect cells against apoptosis, which activates EGFR's downstream signalling pathways, including PI3K, Ras-Raf-MAPK and JNK (Appert-Collin, Hubert, Crémel, & Bennasroune (2015). In more than 30% of cases of inflammatory breast cancer (IBC), a very aggressive subtype of breast cancer and overexpression of EGFR. Patients with these diagnoses usually have a poor prognosis (Alanazi & Khan (2016).

2.1.3.3 C-Myc gene

The c-Myc gene is on the long arm of chromosome 8 and codes for the transcription factor bHLH/LZ (basic Helix-Loop-Helix Leucine Zipper), which contains the Myc protein domain. In the high-grade, invasive stage of breast carcinoma, overexpression of c-Myc is primarily visible. However, no amplification of c-Myc is in benign tissues (Jung et al., 2017).

2.1.3.4 Ras gene

There are three members in the Ras gene family, known as N-ras, H-ras and K-ras, located on chromosomes 1, 11 and 12, respectively. The overexpression of these three human Ras genes is commonly associated with point mutations, and most are missense mutations found in the coding domain for GTP (guanosine triphosphate) binding. Ras

signal transduction pathway defects are in benign and malignant mammary tissue (van Reesema et al., 2016).

2.1.4 Signs and Symptoms of breast cancer

Most breast cancers present with a mass in the breast, which has a high predictive value for malignancy (Koo et al., 2017). Breast cancer is more likely to be a painless, hard mass with irregular edges, but it may also be tender, delicate, or round. It can also be excruciating. Therefore, it is important to have any new breast mass, lump, or alteration assessed by a trained health care professional. Some potential breast cancer signs include (Figure 2.5); swelling of the whole breast or a section of the breast (even if no lump is felt), dimpling of the skin (sometimes looking like an orange peel), nipple or breast pain, retraction of the nipple (turning inward), nipple or breast skin that is red, dry, flaking or thickened, the discharge of the nipple (other than milk), swelling of the Lymph nodes (A breast cancer may often spread to lymph nodes under the arm or around the collarbone, causing a lump or swelling in such area until the original tumour in the breast is big enough to be felt (American Cancer Society, 2019).

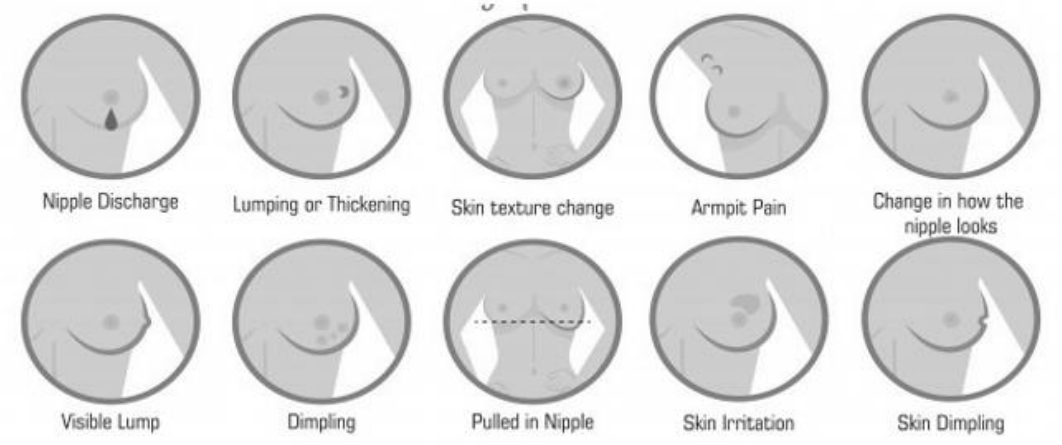


Figure 2.5: Breast cancer signs and symptoms

(Ganesh, 2020)

2.1.5 How common is breast cancer?

Breast cancer is frequent among women universal, and it is a disease with a wide range of molecular subtypes. With an estimated 522,000 deaths yearly, it is the fifth most common type of cancer that causes death in women worldwide (6.4 per cent of the

total). Breast cancer is also a primary cause of death in women living in areas with lower development and income levels by (14.3 per cent of deaths). In regions with higher income indices by 15.4%, breast cancer is the second cause of death after lung cancer. Until menopause starts in women, the risk of breast cancer doubles each decade, which decreases, though it remains common after menopause. The overall survival rates for breast cancer differ by region; nonetheless, the survival rate has increased in recent years due to medical treatment becoming available; hence most breast cancer cases are diagnosed at an earlier and more localized level (American Institute for cancer Research, 2018). Treatment concepts have been developed over the last 10 to 15 years to account for this heterogeneity, focusing on more biologically-directed therapies and medication de-escalation to reduce treatment-related side effects, given the molecular heterogeneity that exists, which is a modern-day care guiding principle. Multimodal therapy advances have improved the likelihood of cure in 70 to 80% of patients (Harbeck et al., 2020).

2.1.6 Advances in breast cancer research

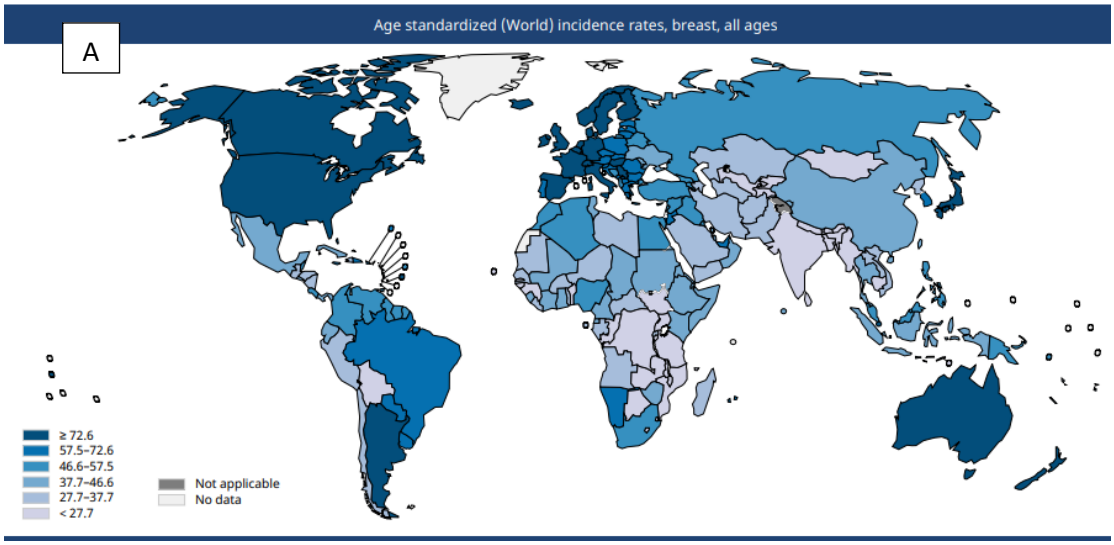
Breast cancer is one of the very few cancers for which there is a reliable screening test, mammography. MRI, ultrasound, and clinical breast tests diagnose breast cancer, but not as a routine screening method. Advances in imaging technology are opening new possibilities for improved screening and early detection, i.e. 3-D mammography, also known as breast tomosynthesis. This technique assembles images from various angles around the breast into a 3-D-like image. While this technology is becoming more commonly available in hospitals, it is uncertain if it is superior to traditional 2-D mammography in detecting cancer earlier. Surgery, chemotherapy, radiation therapy, hormone therapy, and targeted therapy are the pillars of breast cancer treatment. However, scientists are also studying new therapies and medications and new formulations of existing treatments (American Society of Clinical Oncology, 2021) . In a study on breast cancer genetics in African-Ancestry Populations, health disparities research that black females are likely than white females to be diagnosed with aggressive subtypes of breast cancer and die from the disease (Yedjou et al., 2019; Siddharth & Sharma, 2018).

2.2 Breast cancer Epidemiology

2.2.1 Breast Cancer Incidence Worldwide

Above 60 % of newly diagnosed cancers and 70% of deaths are from the ten most common cancer forms. Breast cancer in women is the most prevalent cancer globally, accounting for 11.7 % of all new cases, followed by lung cancer with 11.4 %, colorectal cancer with 10.0 %, Prostate cancer with 7.3%, and stomach cancer with 5.6%. Lung cancer is the primary cause of cancer death by 18.0% of the total cancer deaths, followed by colorectal cancer with 9.4%, liver cancer with 8.3%, stomach cancer 7.7%, and female breast cancer not so far behind with 6.9% (Sung et al., 2021).

Breast cancer is a significant public health concern worldwide. By 2050, the global incidence of female breast cancer is to hit nearly 3.2 million new cases each year (Momenimovahed & Salehiniya, 2019). Figures 2.6 A and B showed breast the incidence and mortality of breast cancer, respectively. Overall, the global burden of cancer incidence and mortality is increasingly high, reflecting both population ageing and growth and shifts in the prevalence and distribution of the primary cancer risk factors, many of which link to socioeconomic development (Sung et al., 2021).



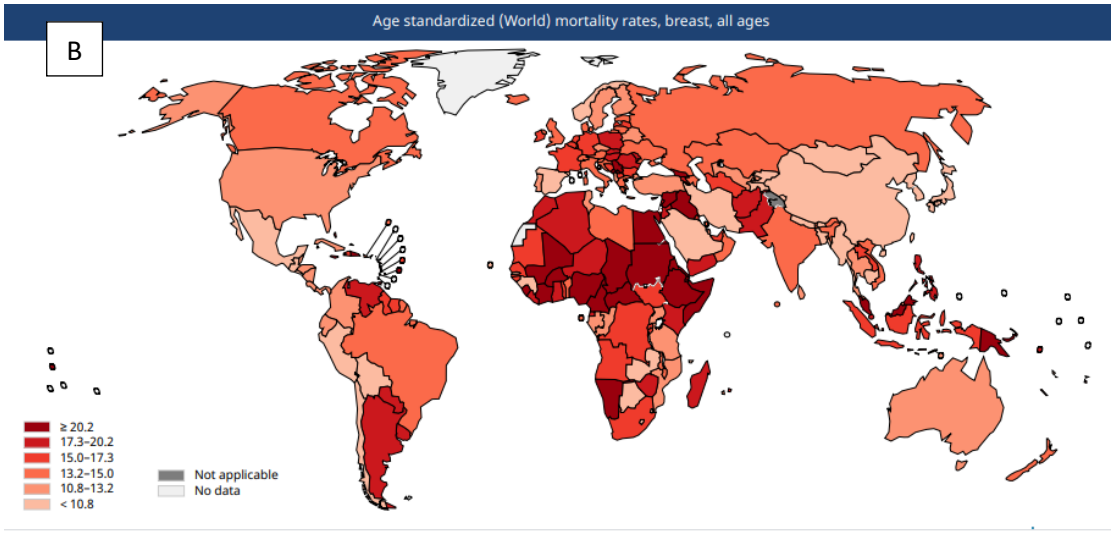


Figure 2.6: Breast cancer incidence and mortality rates in all ages
(Sung et al., 2021)

With 685,000 deaths worldwide, it is the fifth leading cause of cancer death. Breast cancer is the most prevalent cancer in women, accounting for one out of every four cases and every six deaths. It is the most common cancer in most countries (159 out of 185), and it is the most common cause of death in 110 countries (Sung et al., 2021)

In many countries with low and medium human development index (HDI), marked changes in lifestyle, socio-cultural backgrounds, and built environments significantly affect the prevalence of risk factors for breast cancer. The delay of childbearing, fewer children, excess body weight, and physical inactivity are all risk factors. While global breast cancer incidence rates are convergent, mortality rates and survival proportions are lower in settings with lower HDI, owing to late-stage presentation. The Director of IARC, Dr Elisabete Weiderpass, says that "there is an overwhelming need for evidence-based and resource-stratified guidelines that support the phased implementation of breast cancer early detection and treatment into real-world practice" (Portier et al., 2016).

2.2.2 Breast cancer in Africa

Breast cancer amongst others are not uncommon in Africa. Compared to women in developed countries, the likelihood of an African woman living to be of 65 years old is significantly lower. Even if the incidence of breast cancer remains constant, the rise in this likelihood because of increased life expectancy at birth is a significant factor in

Africa's rising breast cancer prevalence. However, the incidence of breast cancer is unlikely to remain stable, and the course of transition is a link to changes in breast cancer epidemiological risk factors (Akarolo-Anthony, Ogundiran & Adebamowo, 2010).

In North Africa, the frequency of breast cancer among women aged 15–49 is lesser than in Western countries. These epidemiological characteristics are primarily the products of unique risk factor profiles, standard in many developing countries and involve rapid changes in reproductive behaviour. These traits have significant consequences for preventing and treating breast cancer (Corbex, Bouzbid & Boffetta, 2014).

Currently, the incidence of breast cancer rates ranges from 19.3 per 100 000 women in Eastern Africa to 89.9 per 100 000 females in Western Europe, with high rates (over 80 per 100 000) in developed regions (excluding Japan) and low rates (less than 40 per 100 000) in most developing regions (Curado, 2011). While advanced countries have the utmost rates of breast cancer incidence and mortality globally, the projected rates in transition countries such as Latin America can rise in prospect. Population-Based Cancer Registries (PBCRs) generate incidence rates worldwide, but they only cover 1 to 5% of Asia, Africa, and South America. As a result, data on the frequency of breast cancer is scarce in these regions due to various factors, including a lack of funding, a lack of priority, and a lack of qualified personnel (Curado, 2011).

Long-term mortality patterns are beginning to diverge, with mortality growing in tandem with the incidence of breast cancer in some nations but dropping in others despite rising incidence rates. Although BC incidence rates are high in affluent countries, fatality rates have declined during the past 25 years. Many causes could cause the rising gap between economically developed and developing countries (Akuoko et al., 2017).

In Africa, knowledge is limited about the complexities of cancer treatment and efforts to improve outcomes. Even though South and North Africa have more resources to combat the liability of breast cancer, both have similar weak prognostic factors. Low and middle-income countries (LMIC) in Africa have a five-year average survival rate for

breast cancer patients that do not exceed 60% (Vanderpuye et al., 2017). Furthermore, despite the advancement made over the last decade, many features remain the same, such as the scarcity of breast preservation treatments, insufficient access to medications, scarcity of oncologists, and the adoption of unhealthy sociocultural practices (Vanderpuye et al., 2017).

2.2.3 Breast Cancer in Namibia

In Namibia, there is an increasing concern over non-communicable illnesses (cancer, diabetes, cardiovascular ailments, hypertension, as a cause of morbidity and mortality, although there is a lack of population-based information in Namibia. The Namibian National cancer registry stated an average of 549 new breast cancer cases per year in 2014-2016 (Namibian National Cancer Registry, 2017). The breast cancer diagnosis figure is high concerning a population of approximately 2 636 625 people alive in Namibia according to the United Nations estimate, 2019. Predominant cancer amongst women in Namibia is breast cancer by 27% of the top 10 most dominant cancers amongst women in Namibia (NNCR, 2017), as shown in Figure 2.7. Breast cancer in Namibia in the years 2010 to 2014 was most common amongst the white women population with 44.7%, but this could also be subject to awareness-based of social-cultural differences and beliefs amongst Namibian women. Furthermore, the NNCR (2017) argued that breast cancer then was not a reportable disease, and complete case data in Namibia may not be possible due to past experiences of incomplete data or inaccuracy in recording region of residence data.

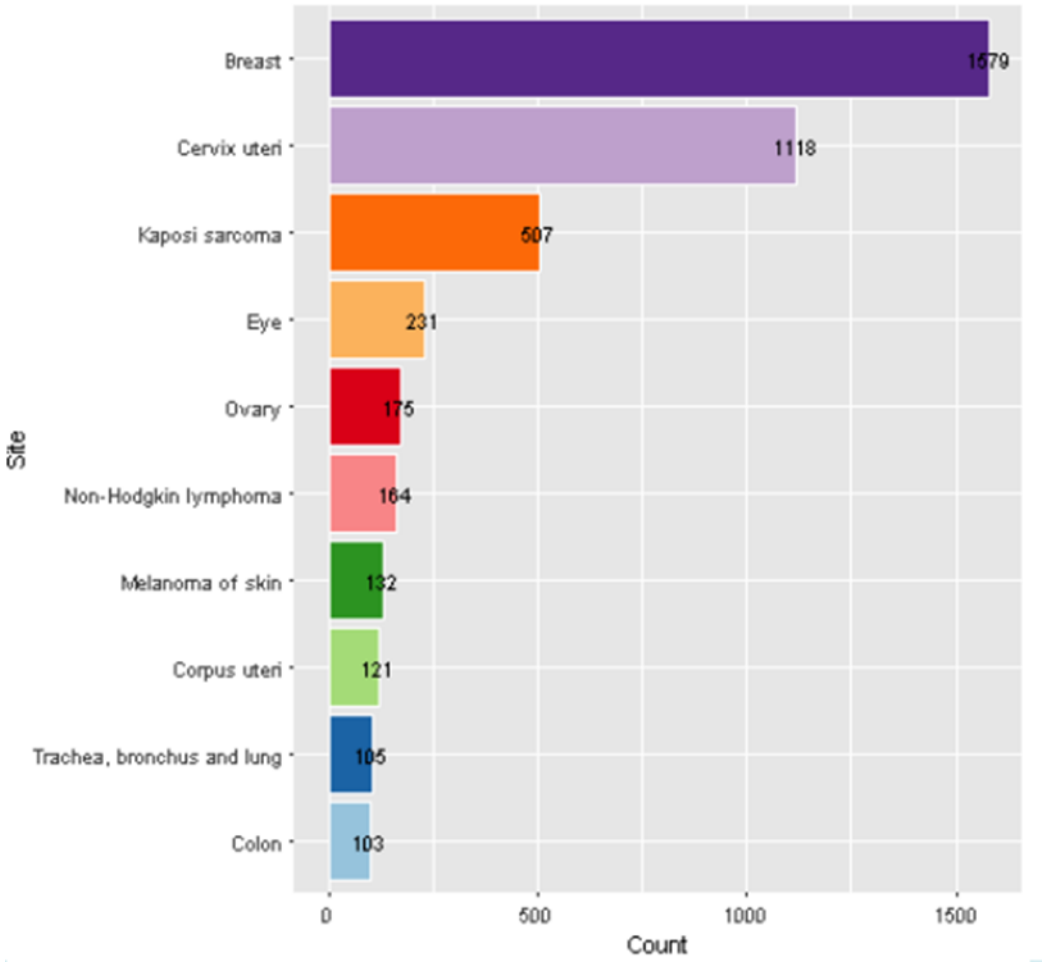


Figure 2.7: Leading cancers amongst females in Namibia. Breast cancer rated first and colon cancer the last as demonstrated by the graph NNCR, (2017).

2.2.4 Breast Cancer risk factors

A breast cancer risk factor can produce a role in increasing the chances of developing a disease (Alam, 2006). Risk factors often present separately, but they do not exist alone in practice. Risk factors often coexist with one another. The existence of risk variables for breast cancer does not imply that cancer is unavoidable; many females with risk variables for breast cancer have no breast cancer diagnosis. At least risk factors help classify women that may profit from screening or other preventative measures (Lakshmi, Athira, Mary & Vijayalakshmi, 2012).

Additionally, all risk factors that initiate the process of breast cancer development consist of two groups. The first set would comprise intrinsic factors such as age, gender, ethnicity, and genetic makeup encouraging the incidence of neoplastic disease in the

family or the existence of mammary gland benign proliferative lesions. They all establish self-determining parameters, and they do not undergo simple modifications during an individual's life. The second set would include extrinsic variables like lifestyle, diet or long-term health intermediation such as the use of oral hormonal contraceptives or hormonal replacement therapy (HRT), and their impact on the neoplastic system can change to some extent (Kamińska, Ciszewski, Łopacka-Szatan, Miotła & Starosławska, 2015). The list of potential factors does not end with the ones listed above. The mentioned breast cancer risk factors only highlight the complex nature of the epidemiological, molecular, and clinical studies.

2.2.4.1 Intrinsic breast cancer risk factors

Age: is a very important basic factor in the diagnosis of neoplastic disease. Women around menopause have been found frequently diagnosed with breast cancer. Breast cancer is less frequent in women below the age of 45 (Kamińska, 2015). Most breast cancers are discovered after menopause; approximately 75% of breast cancer cases occur after the age of 50. Age is thought to be a good proxy for DNA damage sustained over a lifetime (National Breast and Ovarian Cancer Centre, 2009).

Gender: Breast cancer is mostly, but not necessarily, a female-specific illness (Trichopoulos, 2008). It is apparent breast cancer is 100 times more common in females than in men (National Breast and Ovarian Cancer Centre, 2009). A study done by de Block, 2019 in the Netherlands concluded that breast cancer is most frequent in transgender females than in cisgender men, but transgender men have a lower risk of breast cancer than cisgender women. The risk of breast cancer increases in transgender women within a relatively short period of starting hormone treatment, and the breast cancer's characteristics approximated a more female pattern. These findings implied that breast cancer screening criteria for cisgender people are adequate for transgender people who use hormone therapy (de Blok et al., 2019).

Height: a study done by Zhang et al. (2015) showed clear confirmation that adult height is a risk of breast cancer in females and some hereditary factors and biological processes influencing adult height play a key role in the aetiology of breast cancer. Women with height ranging from (≥175 cm vs. <160 cm) are at modestly great risk (National Breast and Ovarian Cancer Centre, 2009). Another study's findings indicated that height under

151 cm was less than those between 151-160 cm with a tendency for better survival in taller persons but no substantial disparity between height groups. A small number of patients and a lack of evaluation of clinical and pathologic parameters as well as anthropometric measurements in the patient population could be the cause for the absence of significant results (cihan, 2017).

Ethnicity: A cohort study done in the United States of America (USA), (2010) assessed differences across racial/ethnic subgroups of women, they concluded that Native American / Alaska, Asian Indian / Pakistan, Black, Filipino, Hawaiian, Mexican, Puerto Rican, and Samoan females are more likely to develop Stage IV breast cancer than non-Hispanic white women and this with a range from 1.3 to 7.1 times higher. Almost all groups were more likely to be diagnosed with oestrogen receptor-negative / progesterone receptor-negative (ER / PR) disease, with the highest odds ratios for black and Puerto Rico women compared to non-Hispanic whites 2.4 times and 1.9 times increase, respectively. Finally, black, Hawaiian, Puerto Rican, and Samoan patients had a 1.5 to 1.8-fold increased risk of breast cancer-specific mortality. Breast cancer differences persist by race / ethnicity, but there are significant differences within the women's subgroup.

Genetics (family History): Family history is a well-known and noteworthy breast cancer risk factor. Women who have a breast cancer-affected mother, sister, or daughter are at twice the risk as those who have no affected first-degree parent. When three or more first-degree relatives are involved, the risk more than triples compared to women who have no affected first-degree relatives. When a close relative is diagnosed with breast cancer at an early age and the family is of Jewish origin, the risk associated with family history increases even further. Some rare deleterious mutations in genes like BRCA1 and BRCA2 are linked to a high risk of evolving breast cancer. Since ovarian cancer is linked to these genes, a family history of ovarian cancer raises the risk of breast cancer. Furthermore, common variants in other genes are each linked to a minor increase in risk (National Breast and Ovarian Cancer Centre, 2009).

2.2.4.2 Extrinsic breast cancer risk factors

Weight: Breast cancer is now widely regarded as a lifestyle condition. The reports on the relationship amid obesity and breast cancer are controversial. Obesity links to a higher

risk of breast cancer in postmenopausal females, but the relationship in premenopausal women is reverse. On the contrary, in a study done in the Southern part of Rajasthan in India, there was no significant association between obesity and breast cancer (Sethi, 2015). Other studies concluded that obesity has links to a lower risk of aggressive breast tumours (Nattenmüller et al., 2018; Thomson, 2012). Physical activity: Amongst premenopausal women, physical exercise correlates to a lower risk of developing breast cancer. Intense recreational physical activity and moderate recreational physical activity protect against breast cancer. Physical exercise appeared to be associated with a lower risk in leaner women than in obese women (Eliassen, 2010; McTiernan et al., 2003).

Ekenga, Parks & Sandler, (2015) concluded that occupational activity correlates to a lower risk of breast cancer. An occupational exercise is a form of physical activity that needs to be looked at further in postmenopausal breast cancer risk studies. Another study concluded that employment category and occupational activity correlates to the probability of developing breast cancer. Office employees and women who sit for long periods at work tend to be at a greater risk (Sari et al., 2020).

Diet: According to the available evidence, low-fat and high-fibre diets may be weakly protective against breast cancer, while overall energy intake and alcohol consumption tend to be positively related. Fibre can be weakly protective, likely due to oestrogen regulation, while fruit and vegetable consumption does not correlate to the risk of breast cancer. Diet appears to be modestly associated with breast cancer risk; correlations are more pronounced for postmenopausal disease, and healthier choices following diagnosis and treatment are likely to promote endurance more than reduced risk of recurrent (Ruiz, 2014; Thompson, 2012).

In addition, Ruiz and Hernandez (2014) argued that diet is responsible for 30–35 % of the risk factors that lead to cancer. Some foods and eating habits are related to an increased risk of cancer. However, available epidemiological evidence for several foods is inconsistent, and the associations with cancer risk remain unknown. Epidemiological studies will help fully understand this problem in the future. The lifestyle factor most consistently linked to an increased risk of breast cancer is alcohol intake (Jung et al., 2016). Many studies have shown that regardless of the type of alcoholic beverage consumed, women who drink much alcohol have a 40–50% higher risk of breast cancer than abstainers Jung et al. (2016), Smith-Warner et al. (1998), Chen (2011) & Allen at el. (2009). There is also a dose-response relationship between alcohol consumption and

breast cancer, with each 10 g of alcohol consumed per day increases the risk of breast cancer by 9–12% (Smith-Warner, 1998; Allen, 2009).

Hormone replacement therapy (HRT): At the median age of 51, women usually experience a physiological event called menopause. Hormone replacement therapy (HRT) comprises oestrogen to dismiss menopausal symptoms and is paired with a progestogen to treat endometrial cancer in women who still retain their uterus (Hickey, Elliott & Davison, 2012). There is strong evidence that adding progestin to HRT increases the risk of breast cancer significantly compared to oestrogen alone. These results have significant implications for the risk-benefit analysis of HRT with the usage of combination hormone replacement therapy (CHRT) by women (Ross, 2000). In a realistic perspective study on HRT and breast cancer risk, the use of conjugated equine oestrogen (CEE)/ medroxyprogesterone acetate (MPA) correlates to a rise in breast cancer incidence and mortality (Stevenson, 2011).

Hormonal factors: Exogenous (taken in some form) and endogenous (made by one's body) hormones play a role in determining the risk of breast cancer. These factors include;

- Menopause over 55 years of age
- Current users of HRT
- With the use of the contraceptive pill, the risk decreases by ten years after ceasing use
- Menarche before the age of 12
- High levels of androgens circulating up to 20 % for both pre and postmenopausal women
- High level of insulin-like growth factors circulating, women with levels in top 25% probably only for postmenopausal women
- Diethylstilboestrol use during pregnancy
- Diethylstilboestrol in utero exposure

Pregnancy and birth weight (Trichopoulos, 2008) confirmed that regardless of the woman's age, a pregnancy divulges a short-term increase of breast cancer risk Following that, there is a significant long-term reduction in this risk, as was originally established in a famous international epidemiological study on the first pregnancy some 40 years ago by (MacMahon et al., 1970). Pregnancy affects the breasts dramatically, making it

less probable for breast cells to grow and for tumours to form. This could explain why pregnancy has a protective impact on younger women. However, why becoming a first-time mother at a later age has the opposite effect is unknown. Breast tissue is more prone to acquire cells harbouring cancer-causing mutations, or clusters of aberrant cells with the potential to become malignant, after the age of 35; though, it is unclear how these cells were altered by a late-age first pregnancy (Chakravarthi & Varambally, 2013). It is apparent that that the answer to this issue can be found in the JAK-STAT5 signalling pathway according to (Haricharan et al., 2013).

High birth weight associates with a higher risk of breast cancer in the offspring (Trichopoulos, 2008). In addition to what was mentioned earlier by Trichopoulos, Bukowski, 2012 concluded that giving birth to an infant with high birth weight was linked to an increased risk of breast cancer later in life, regardless of the mother's birth weight or breast cancer risk factors and was also linked to a hormonal environment favouring forthcoming breast cancer development and progression during pregnancy. High birth weight first pregnancies may raise the risk of breast cancer, probably due to the relationship between birth weight and oestrogen levels and insulin-like growth factor 1 (Swerdlow, 2018).

Factors such as increased number of births compared to 1 birth are associated with decreased risk for breast cancer (National Breast and Ovarian Cancer Centre, 2009). Each pregnancy at a young age, not only the first, is linked to a considerable long-term breast cancer preventive benefit. Furthermore, only 34 weeks or more pregnancies link to a lower risk of breast cancer. Breast cancer risk reduces regardless of whether the pregnancy resulted in a stillbirth or live birth, and hence nursing cannot be blamed; this implies that during week 34 of pregnancy, a unique biological response produces long-term breast cancer prevention (Husby, Wohlfahrt, Øyen & Melbye, 2018).

Environmental Factors: Environmental factors presumably cause a large portion of breast cancer. Breast cancer correlates to ionizing radiation, a well-known environmental risk factor. Chemicals that cause mammary cancer in rodents are human study subjects; however, occupational and environmental exposure to these chemicals is unrelated to breast cancer risk (Coyle, 2004).

2.3 Breast Cancer Detection and Screening

Discovering breast cancer happens after symptoms occur mainly, although people with breast cancer disease often have no signs or symptoms. Therefore, it is vital to get screened for breast cancer regularly. Screening is a term used to describe tests and examinations to detect an illness in people who have no symptoms. Breast cancer can be detected and diagnosed using a variety of tests or modalities. These include mammograms, Breast Ultrasound, Breast MRI scans, and biopsies. Tests assess if breast cancer has spread, usually chest x-rays, CT scans, bone scans, PET scans, and MRI scans (American Cancer Society, 2017). Breast cancer risk assessment is usually before breast screening.

2.3.1 Breast Cancer Risk Assessment

Breast cancer risk assessment is critical for recognizing women who may benefit from more comprehensive breast cancer observations; however, there seems to be no systematic method to office-based breast cancer risk assessment in Namibia. Lack of risk assessment may result in overlooked opportunities to recognize women at high risk of breast cancer and apply average-risk screening guidelines to high-risk women.

Risk evaluation and recognition of high-risk women allows for referral to healthcare professionals who specialize in cancer gene therapy and monitoring for breast cancer-related germline mutations (e.g., BRCA), patient counselling on risk-reduction options, and cascade testing to classify family members who may also be at risk (American College of Obstetricians and Gynaecologists, 2017). Although departments such as medical Imaging have some form of risk assessment for breast cancer screening, risk assessment prior to referral to imaging departments are unknown for other breast screening departments.

2.3.2 Breast assessment tools

Two main things to consider when assessing a woman's risk for breast cancer are, her chances of having a high-risk gene such as BRCA1 and BRCA2 genes and her risk for developing breast cancer without such mutations. The combination of these risks and the risks and benefits of the intervention will decide whether the intervention is appropriate. Several breast cancer assessment tools validate the risk to a certain

degree. Risk assessment allows greater accuracy in determining which women are most likely to develop breast cancer. In addition to the probability of BRCA1 and BRCA2 genes, the risk assessment tool calculates the chances of breast cancer developing over a given lifetime. Although some risk-assessment tools answer only one of the questions, many often provide a result for the other. The Tyrer- Cuzick model measures breast cancer risk over a while, but it does provide a readout for the individual's BRCA1/2 probability Evans & Howell , (2007).

2.3.3 The Tyrer-Cuzick Model

It is vital to provide an accurate risk assessment for breast cancer to personalize screening and risk mitigation strategies. The Tyrer Cuzick model predicts a 10 –year risk of breast cancer development. According to a study done by Boughey et al., (2010), , individual risk estimates showed weak concordance between projected risk and invasive breast cancer growth, and the Tyrer-Cuzick model significantly overestimated breast cancer risk for women with atypia.

Overall, the Tyrer-Cuzick model is a well-studied and widely available model for predicting breast cancer amongst all the models for detecting breast cancer risk. Only the Tyrer-Cuzick model accounts for personal and comprehensive family history risk factors.

Annual screening breast MRI should be considered if a woman's lifetime risk is greater than 20% after the Tyrer Cuzick calculation. Since mammography can miss certain breast cancers, breast MRI should be an addition to annual mammography. It is important to remember that estimating lifetime risk is not the only part of a risk evaluation and that ordering a screening breast MRI is not the only way to protect or track women at high risk. Women at high-risk benefit from risk reduction measures such as lifestyle changes, chemoprevention, and breast MRI screening (Himes, 2016).

2.4 Breast Cancer Screening Modalities

2.4.1 Breast Self-examination (BSE)

An early step to help prevent breast cancer is for women to perform this procedure. BSE does not require an individual to go to the hospital or clinic. BSE requires an individual to assess their breast to physically detect changes in the breast. The BSE method is cost-efficient and only requires discipline from an individual. On the other hand, if women do

not notice any lumps during BSE, they will not undergo further breast screening because they are confident that their breasts are free of imperfections. Regardless, BSE could still save the lives of those women that could have breast cancer (Ali, 2018). In a study (Al-Sharbatti, Shaikh, Mathew & Al-Biate, 2013), the lack of knowledge about how to do BSE and the lack of doctor advice were the most common deterrents to BSE. A quarter of the respondents believed they were at risk for breast cancer, with around half believing their risk was minimal, this could be similar for Namibian women, and it is an area worth exploring.

2.4.2 Mammography

Mammography screening uses X-ray imaging to detect breast cancer. The breasts are compressed during the x-ray to enable the radiologist to see irregular masses more clearly. There is radiation exposure with mammograms, typically less than 20% of annual background radiation. Mammography divides into two types: screening and diagnostic. Today, screening mammography is the traditional breast cancer screening test. When done at recommended intervals, mammographic screening for breast cancer is beneficial. Unfortunately, not all women are subject to the same screening level due to financial constraints, a lack of knowledge and education, physical limitations, living in rural areas, and a lack of encouragement from doctors (Tariq, Khubaib, Imran & Ibrahim 2011).

Mammograms have their downside as they can miss some cancers; in some cases, women need more tests to find if something on the mammogram is cancer or not. There is a chance a patient will be diagnosed with cancer that would never have caused any complications if not discovered through screening. Women who have mammograms must be aware of what to expect and aware of the benefits of screening (Qin, Nagler, Fowler & Gollust, 2019).

The only procedure currently considered appropriate for mass screening of asymptomatic women is mammography screening. However, its widespread use necessitates a thorough examination of possible side effects. Since the risk of radiation is much lower than the natural annual risk of breast cancer, it should not be a reason to avoid screening. In addition, false-positive calls necessitate further imaging or histopathological evaluation, most commonly a percutaneous breast biopsy (Heywang-Köbrunner,Hacker & Sedlacek, 2011). Routine mammographic positioning aims to

screen the whole breast thoroughly. In the two-projection mammogram, in most situations, the finest covering of the breast tissue is provided by the cranial-caudal (CC) and mediolateral oblique (MLO) projections.

2.4.3 Breast Ultrasound

The use of breast ultrasound in the diagnosis of breast lesions is essential. It is the primary modality for examining anomalies in young women (under 30 years old). Ultrasound identifies mammographic abnormalities as solid or cystic and guides image-guided breast interventions. The use of ultrasound has changed in recent years. It is gaining confidence as a critical screening method for females with dense breast tissue. Due to the limitations of mammography in women with dense breast tissue, further screening with ultrasound and magnetic resonance imaging has turn out to be available (Rapelyea & Marks, 2018).

For women at high risk of breast cancer, adding a single screening ultrasonography test to mammography increases the identification of breast cancers that are often small and node-negative (Berg et al., 2008). According to American College of Radiology (ACR) appropriateness guidelines, ultrasound is an adjunct to mammography for mass characterisation and is the following test to characterise a mammographic mass (Harvey et al., 2013). If a breast ultrasound mass is assumed to be related to a mammographic mass, the scale, shape, location, and surrounding tissue composition should be similar in both modalities (Whitman, Arribas & Uppendahl, 2011).

If no sonographic correlation for a mass is on a mammogram, the mammogram re-evaluation is necessary. Suppose mammographic findings remain suspicious for an ultrasound occult mass. In that case, considering further evaluation with a different imaging modality or biopsy is necessary (Rapelyea, 2018). shown in Figure 2.8 Images A and B are mammograms images of a patient with a lump shown in different views, “A” is a right breast CC view, “B” is a right breast MLO view and “C” is an ultrasound image presenting a lump of the same patient. Note how the two different modalities present the same mass in Figure 2.8.

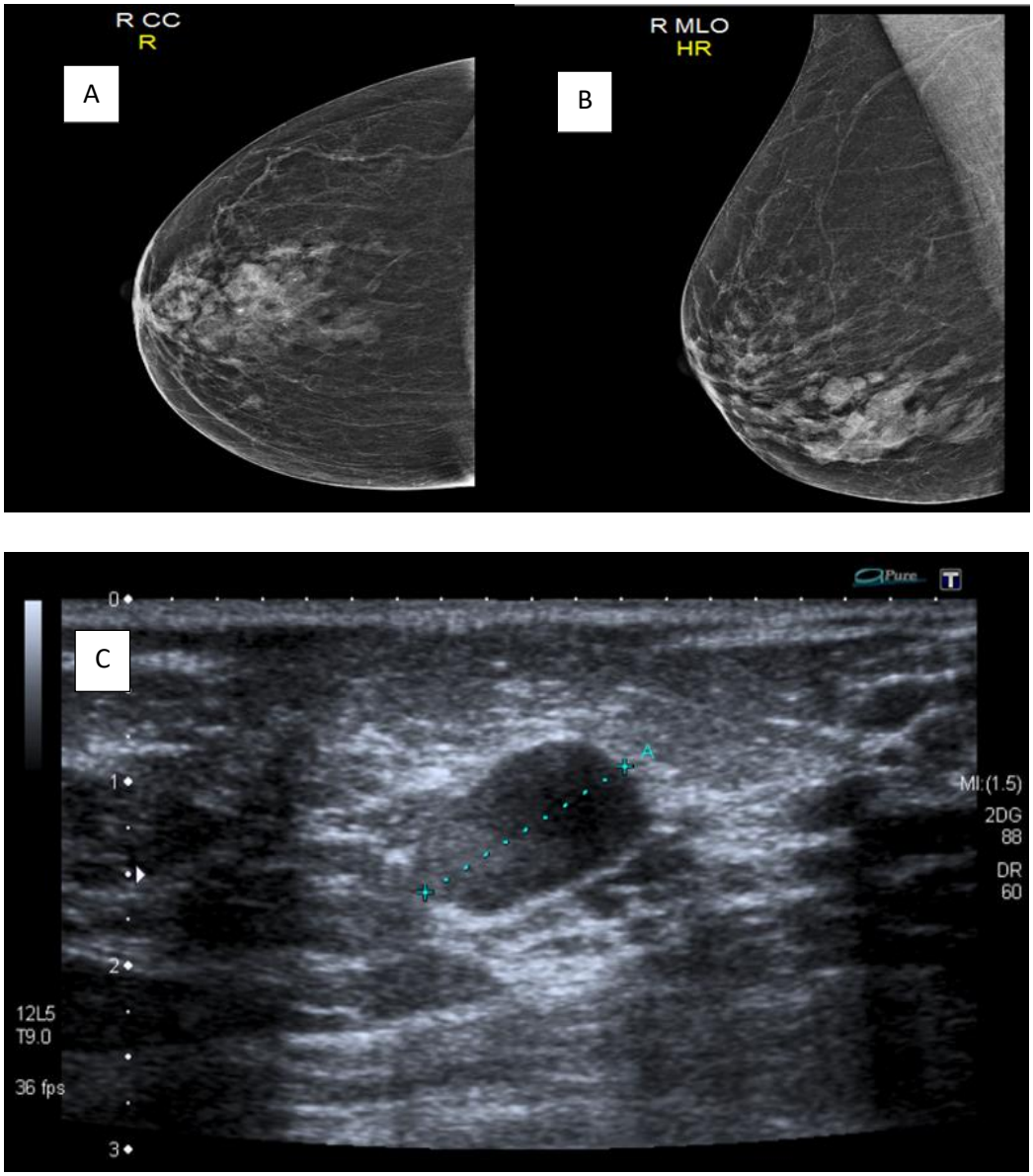


Figure 2.8: Above are images of a female patient with age above 40, clinical history of a palpable mass in the right breast. Images "A" and "B" are lobulated nodular changes retro areolar in a central position of the right breast on a mammogram CC and MLO views respectively**.** Image "C" demonstrates a sonographic evaluation. Inferolateral to the right nipple an ovoid solid nodular structure evident measuring 13 x 8 mm in size with a relatively vertical orientation containing complex fluid or is solid. (Medical Imaging, 2020).Printed with permission.

2.4.4 Breast Magnetic Resonance Imaging (MRI)

A regular MRI system with a special connection ('breast coil') conducts a breast MRI. The patient position is prone for the procedure, and images before and after the rapid

injection of gadolinium, a contrast medium. Reporting breast MRI requires the expertise of a specialized radiologist and includes analysis of the form of enhancement and the morphology of lesions, as well as the kinetic features. When an MRI reveals a suspected lesion, a 'second look' on ultrasound can determine a biopsy if a lesion is still visible (Brennan, Spillane & Houssami, 2009).

There is strong evidence that MRI identifies supplementary cancers not seen on mammography plus ultrasound while screening people with a high genetic risk of breast cancer. For women at average risk of breast cancer, there is no proof that MRI is a stand-alone screening test. MRI is used to measure the level of disease in women who have recently been diagnosed with breast cancer and to identify contralateral disease that is not visible on traditional imaging. Women with breast symptoms should undergo the traditional triple test (clinical examination, mammography and ultrasound screening, and percutaneous needle biopsy (Brennan et al., 2009).

Along with mammography and ultrasound, breast MRI is an important modality. Its key indications are cancer staging, breast cancer screening in high-risk women, and neoadjuvant chemotherapy response assessment. MRI is a practical procedure, unlike mammography and ultrasound. The penetrability of blood vessels is assessed using contrast material–enhanced MRI, which uses an intravenous contrast agent (gadolinium chelate) to shorten the local T1 time, resulting in a higher signal on T1-weighted images. The basic idea is that neoangiogenesis causes the development of leaky vessels, which rises contrast agent extravasation, resulting in rapid local enhancement (Mann, Cho, and Moy, 2019). Fig 2.9 shows an MRI image demonstrating a clear contrast-enhanced tumour.

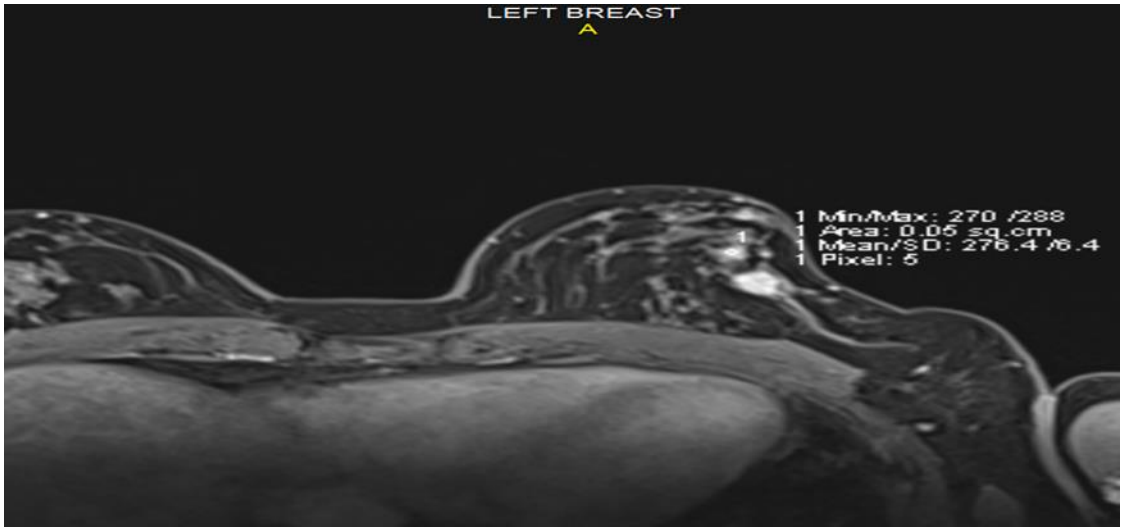


Figure 2.9: MRI chest wall image is of a 62-year-old female patient breast. Patient had Type c (heterogeneous fibro glandular tissue) with a background parenchymal enhancement: moderate and symmetrical. Image above demonstrating a mildly nodular enhancing lesion detected within the central lateral breast, measuring approximately 10.9mm (transverse) x 9.0mm (AP) x 12.0 mm. This nodule was confirmed to be breast cancer after biopsy results. (Medical Imaging, 2020). Printed with permission.

2.4.5 Breast Biopsy

Breast pathology diagnosis determines clinical treatment and management decisions (Elmore et al., 2015). It is a safe and cost-effective process that allows for an accurate diagnosis, essential for sound decision-making, including treatment preparation when necessary. Diagnostic surgical excisions, associated with a more extended hospital stay, higher cost, and potential complications, have been replaced by percutaneous image-guided breast biopsies. There are different breast tissue sampling/biopsies (Bick et al., 2020).

In addition, Fine-needle sampling (FNS), core needle biopsy (CNB), and vacuum-assisted biopsy (VAB) coexist nowadays, with the first providing material for cytological analysis and the latter two providing material for tissue examination (histopathological examination). These techniques can operate by mammography tomosynthesis, ultrasound, or MRI. FNS and CNB, on the other hand, should be used according to US guidelines, whereas VAB works according to tomosynthetic-mammography or MRI guidelines. These common combinations are due to a variety of technical factors, such as visibility at each technique and the types of lesions identified (Bick et al., 2020).

The different types of needle sampling entail the follows;

Fine needle sampling/ Fine needle aspiration biopsy (FNS/FNAB)

In local chest wall recurrence evaluations and lymph node metastasis and inoperable disorders, FNAB is an appealing alternative to surgical biopsy. FNAB is also useful for sampling tumours and evaluating surrogate endpoint biomarkers in chemoprevention trials. However, because of the high incidence of unsatisfactory samples, the lack of qualified cytopathologists, and the inability to evaluate non-palpable breast lesions, the involvement of FNAB in the evaluation of non-palpable breast lesions is questioned to distinguish between in situ and invasive disease (Nassar, 2011). A fine needle with a diameter ranging from 18 to 27 gauge (same or identical to those used for intramuscular injections) inserted very close to the ultrasound (US) probe. Once the needle is visible within the mark, manual multidirectional sampling occurs, either by aspiration with a 10-20-mL syringe or a vacuum aspiration device (fine-needle aspiration) or simply by manual movement of the needle (Bick et al., 2020).

Vacuum-assisted biopsy (VAB)

During this procedure, needles ranging from 12 to 7 gauge are necessary, with the latter being the most significant size commercially available for a percutaneous breast biopsy (Bick et al., 2020).

Stereotactic biopsy

Stereotaxis is a method for determining the three-dimensional location of a breast abnormality. It helps identify lesions such as microcalcifications, suspicious asymmetries, and small nodules from the biopsies. The use of an add-on digital mammography kit helps the radiologist measure the exact 3-D position of the lesion using only a low-dose X-ray, which is why this procedure is recommended for microcalcifications, as shown in Figure 2.10. an x-ray of the sample to verify capturing microcalcifications is considered (Glenn & Andrea, 2017).

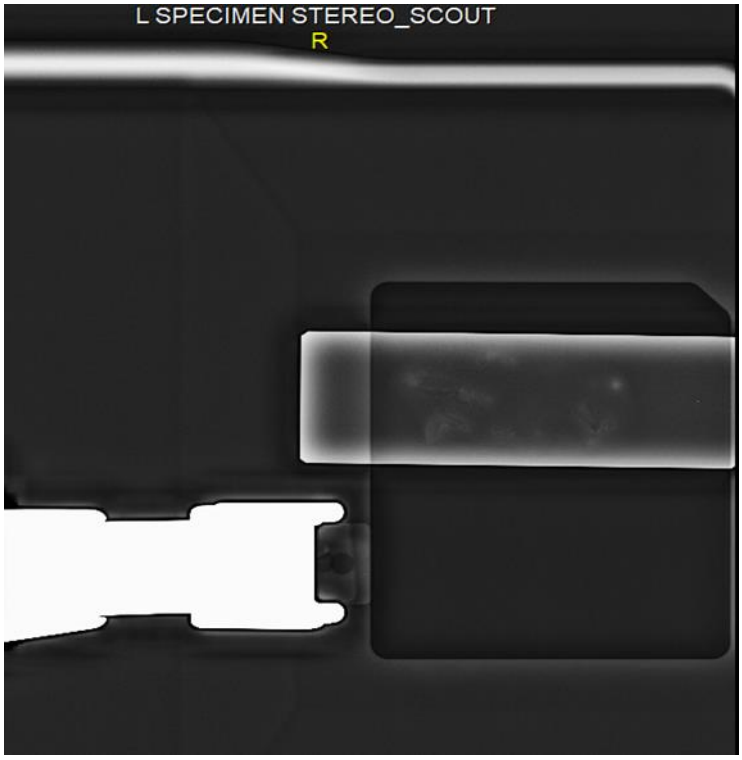


Figure 2.10: An x-ray of the tissue strands from female patient on a slide after the stereotactic biopsy was performed. (Imaging, Medical, 2020).Printed with permission.

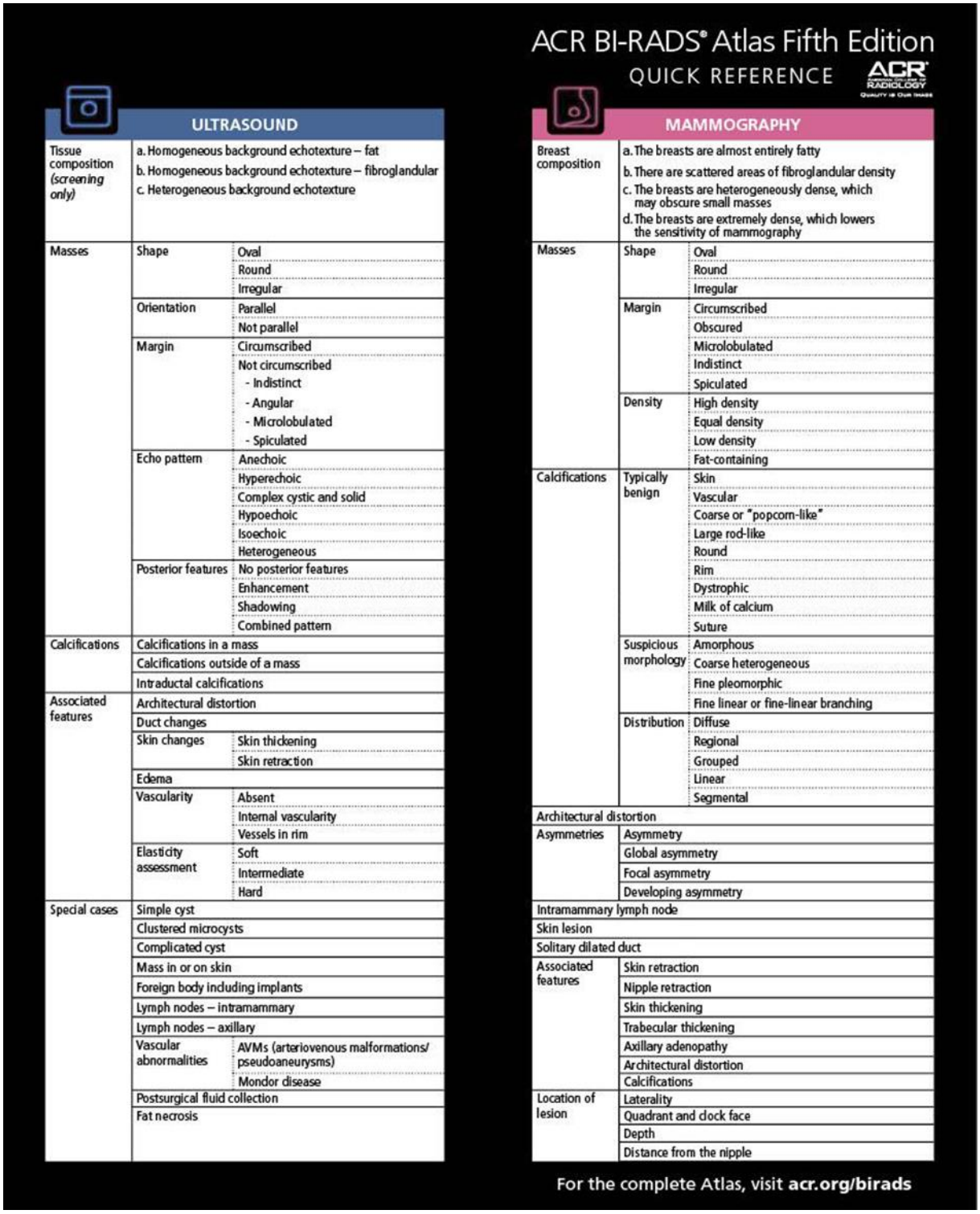
Hook-wire Localization

Wire localization of non-palpable mammographically diagnosed breast lesions is a well-established technique whose significance has increased in recent years as mammography has become more widely used in the investigation of symptomatic breast disease. Accurate localization is crucial to effectively manage these non-palpable lesions, which calls for complete surgical excision with optimal cosmetics and minimal morbidity. Mammograms and sonography are the most widely used imaging guidance techniques. Although the use of MRI and CT scans are less frequent, wire localization is a well-established method for treating impalpable breast lesions (Jakimovska Dimitrovska, 2015)

2.4.6 Breast Imaging Reporting and Data System (BI-RADS) classification system

Breast Imaging Reporting and Data System (BI-RADS) is a structured system for reporting breast pathology seen on mammograms, ultrasounds, and magnetic resonance imaging (MRI). This well-organized method promotes continuity in reports and other documents, providing a lexicon of descriptors, a reporting system that links

evaluation categories to management recommendations, and a data collection and auditing mechanism to promote direct contact between the radiologist and other physicians in Figures 2.11 and 2.12. The 5th version of BI-RADS, published in 2013, brought many updates to achieve specific objectives. Multiple new descriptors reflect the increasing danger of malignancy that an image finding reflects. Historic descriptors have withdrawn due to underutilization or redundant use, and pre-existing descriptors have changed their names to match definitions across the three imaging modalities (Spak et al., 2017).



ACR BI-RADS® Atlas Fifth Edition

QUICK REFERENCE

ACR RADIOLOGY

ULTRASOUND

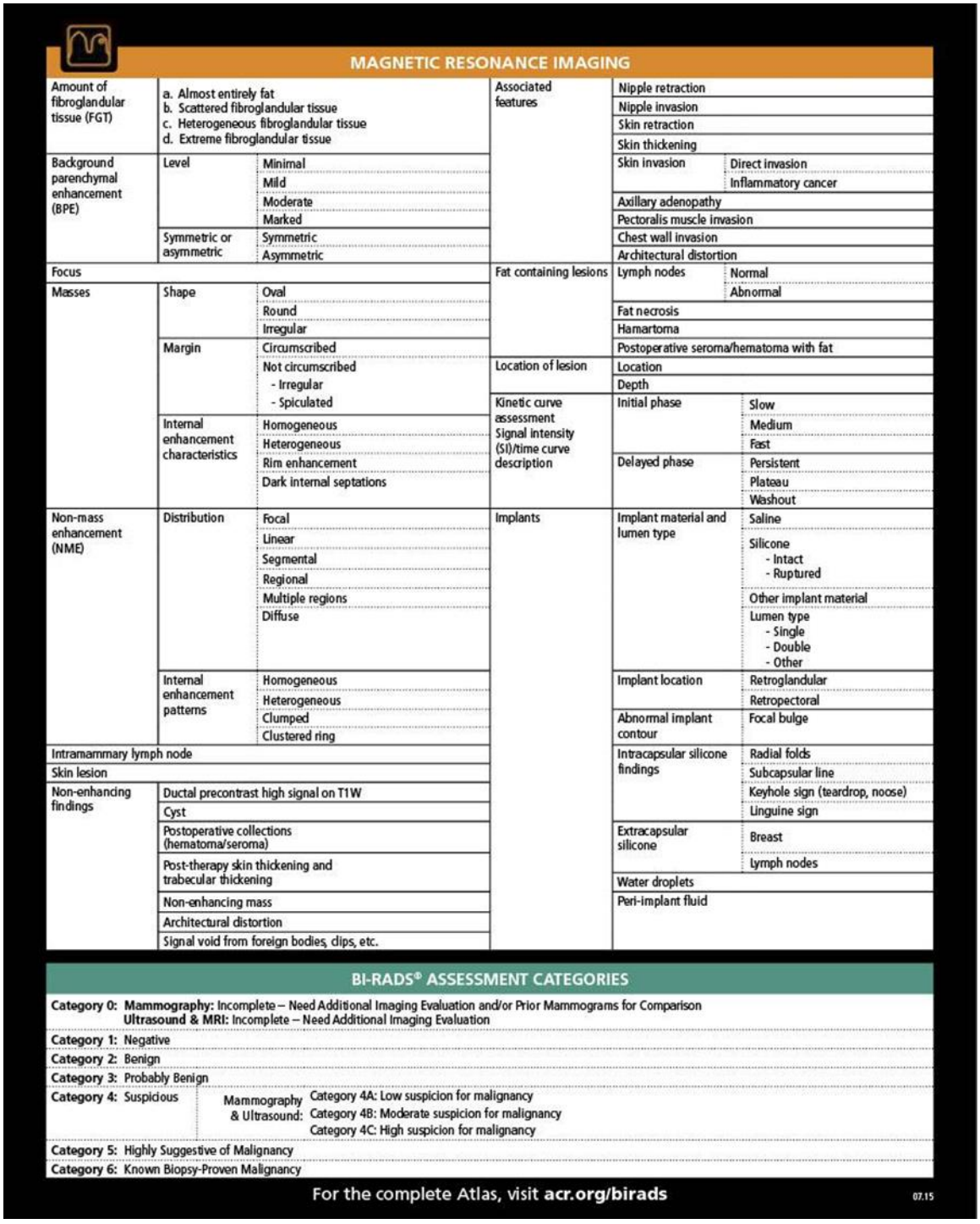
Tissue composition *(screening only)*	a. Homogeneous background echotexture – fat b. Homogeneous background echotexture – fibroglandular c. Heterogeneous background echotexture	
Masses	Shape	Oval
		Round
		Irregular
	Orientation	Parallel
		Not parallel
	Margin	Circumscribed
		Not circumscribed - Indistinct - Angular - Microlobulated - Spiculated
	Echo pattern	Anechoic
		Hyperechoic
		Complex cystic and solid
		Hypoechoic
		Isoechoic
		Heterogeneous
	Posterior features	No posterior features
		Enhancement
		Shadowing
		Combined pattern
Calcifications	Calcifications in a mass	
	Calcifications outside of a mass	
	Intraductal calcifications	
Associated features	Architectural distortion	
	Duct changes	
	Skin changes	Skin thickening
		Skin retraction
	Edema	
	Vascularity	Absent
		Internal vascularity
		Vessels in rim
	Elasticity assessment	Soft
		Intermediate
		Hard
Special cases	Simple cyst	
	Clustered microcysts	
	Complicated cyst	
	Mass in or on skin	
	Foreign body including implants	
	Lymph nodes – intramammary	
	Lymph nodes – axillary	
	Vascular abnormalities	AVMs (arteriovenous malformations/ pseudoaneurysms)
		Mondor disease
	Postsurgical fluid collection	
	Fat necrosis	

MAMMOGRAPHY

Breast composition	a. The breasts are almost entirely fatty b. There are scattered areas of fibroglandular density c. The breasts are heterogeneously dense, which may obscure small masses d. The breasts are extremely dense, which lowers the sensitivity of mammography	
Masses	Shape	Oval
		Round
		Irregular
	Margin	Circumscribed
		Obscured
		Microlobulated
		Indistinct
		Spiculated
	Density	High density
		Equal density
		Low density
		Fat-containing
Calcifications	Typically benign	Skin
		Vascular
		Coarse or "popcorn-like"
		Large rod-like
		Round
		Rim
		Dystrophic
		Milk of calcium
		Suture
	Suspicious morphology	Amorphous
		Coarse heterogeneous
		Fine pleomorphic
		Fine linear or fine-linear branching
	Distribution	Diffuse
		Regional
		Grouped
		Linear
		Segmental
Architectural distortion		
Asymmetries	Asymmetry	
	Global asymmetry	
	Focal asymmetry	
	Developing asymmetry	
Intramammary lymph node		
Skin lesion		
Solitary dilated duct		
Associated features	Skin retraction	
	Nipple retraction	
	Skin thickening	
	Trabecular thickening	
	Axillary adenopathy	
	Architectural distortion	
	Calcifications	
Location of lesion	Laterality	
	Quadrant and clock face	
	Depth	
	Distance from the nipple	

For the complete Atlas, visit **acr.org/birads**

Figure 2.11: Mammography and ultrasound terminology, report organization, assessment structure, and a classification system that are all standardized. (American College of Radiology, 2013)



MAGNETIC RESONANCE IMAGING

Amount of fibroglandular tissue (FGT)	a. Almost entirely fat b. Scattered fibroglandular tissue c. Heterogeneous fibroglandular tissue d. Extreme fibroglandular tissue		Associated features	Nipple retraction	
				Nipple invasion	
				Skin retraction	
				Skin thickening	
Background parenchymal enhancement (BPE)	Level	Minimal		Skin invasion	Direct invasion
		Mild			Inflammatory cancer
		Moderate		Axillary adenopathy	
		Marked		Pectoralis muscle invasion	
	Symmetric or asymmetric	Symmetric		Chest wall invasion	
		Asymmetric		Architectural distortion	
Focus			Fat containing lesions	Lymph nodes	Normal
Masses	Shape	Oval			Abnormal
		Round		Fat necrosis	
		Irregular		Hamartoma	
	Margin	Circumscribed		Postoperative seroma/hematoma with fat	
		Not circumscribed - Irregular - Spiculated	Location of lesion	Location	
				Depth	
	Internal enhancement characteristics	Homogeneous	Kinetic curve assessment Signal intensity (SI)/time curve description	Initial phase	Slow
		Heterogeneous			Medium
		Rim enhancement			Fast
		Dark internal septations		Delayed phase	Persistent
					Plateau
					Washout
Non-mass enhancement (NME)	Distribution	Focal	Implants	Implant material and lumen type	Saline
		Linear			Silicone - Intact - Ruptured
		Segmental			Other implant material
		Regional			Lumen type - Single - Double - Other
		Multiple regions			
		Diffuse			
	Internal enhancement patterns	Homogeneous		Implant location	Retroglandular
		Heterogeneous			Retropectoral
		Clumped		Abnormal implant contour	Focal bulge
		Clustered ring		Intracapsular silicone findings	Radial folds
Intramammary lymph node					Subcapsular line
Skin lesion					Keyhole sign (teardrop, noose)
Non-enhancing findings	Ductal precontrast high signal on T1W				Linguine sign
	Cyst			Extracapsular silicone	Breast
	Postoperative collections (hematoma/seroma)				Lymph nodes
	Post-therapy skin thickening and trabecular thickening			Water droplets	
	Non-enhancing mass			Peri-implant fluid	
	Architectural distortion				
	Signal void from foreign bodies, clips, etc.				

BI-RADS® ASSESSMENT CATEGORIES

Category 0:	**Mammography:** Incomplete – Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison **Ultrasound & MRI:** Incomplete – Need Additional Imaging Evaluation	
Category 1:	Negative	
Category 2:	Benign	
Category 3:	Probably Benign	
Category 4:	Suspicious	Mammography & Ultrasound: Category 4A: Low suspicion for malignancy Category 4B: Moderate suspicion for malignancy Category 4C: High suspicion for malignancy
Category 5:	Highly Suggestive of Malignancy	
Category 6:	Known Biopsy-Proven Malignancy	

For the complete Atlas, visit **acr.org/birads**

07.15

Figure 2.12: Demonstrated above is MRI terminology, report organization, assessment structure, and a classification system that are all standardized. (American College of Radiology, 2013).

2.4.7 Reporting System

The BI-RADS framework allows residents and breast imaging fellowships to interpret mammographic results comprehensively and effectively. The American College of Radiology and the Society of Breast Imaging also suggest that breast imaging residency and fellowship programs entail using BI-RADS terms and assessment categories (Pesce, 2019).

There is a structure to be considered when reporting for breast screening. According to the American College of Radiology (2013), the reporting system should be concise and well-organized (Table 2.1).

Table 2.1: Structure of a Radiological Report (American College of Radiology, 2013)

Report Structure
1. Indication for examination
2. Succinct description of the overall breast composition
3. Clear description of any important findings
4. Comparison to previous examination(s), if deemed appropriate by the interpreting physician
5. Assessment
6. Management

Indication for examination: provision of a brief explanation of the reason for the examination should.

A succinct description of the overall breast composition: this is a general estimate of the amount of attenuating tissues in the breast that can help determine the likelihood that normal tissue covers a lesion and that the test sensitivity will be impaired. Since mammography does not detect all types of breast cancer, clinical breast examination is an essential part of the screening process. Overlooking clinical breast examination findings is not optional, and they may be even more critical in dense breasts. Current evidence does not encourage mammographic breast density to determine the frequency of mammograms.

A clear description of any critical findings: most significant results are either concerning at screening, potentially dubious, fresh, or more extensive comprehensive as compared to previous examinations. Characteristics to consider are mass, calcifications,

architectural distortion, asymmetries, intramammary lymph nodes, skin lesions, and solitary dilated ducts.

Comparison to previous examination(s), if deemed appropriate by the interpreting physician: If the finding of concern necessitates an assessment of change or stability, the comparison to a previous test may be helpful. When a result has unmistakably positive characteristics, the comparison is not necessary. Where a result is potentially suspicious, a comparison can be meaningless to check for malignancy.

Assessment: The Food and Drug Administration's Quality Mammography Standards; Final Rule3 requires the inclusion of an appraisal group in the overall overview of the mammography study (Table 2.2). BI-RADS evaluation categories are concordant with relevant management guidelines, unlike FDA-mandated evaluations, which are not related to management recommendations. Integrating evaluation types with congruent management recommendations improves medical practice even further. All final evaluations (BI-RADS categories 1, 2, 3, 4, 5, and 6) should be based on a detailed inspection of the mammographic features of concern or after a harmful or benign examination. An incomplete (category 0) assessment is generally for screening exams and additional imaging evaluation before a final assessment. At the same time, a category 4 or 5 assessment in the screening environment is on rare occasions. A recall (category 0) evaluation should provide detailed recommendations for the next step (spot-compression magnification views, US, and other modalities.

Management: In the absence of clinical contraindications, the report should state the biopsy performance when there is a suspected abnormality; this is a diagnosis report in which the interpreting doctor is concerned enough to recommend a biopsy based on the imaging findings. The prescribed terminology ("there should be biopsy performance unless there is a clinical contraindication") allows for the rare situation in which the patient or her physician might reasonably wish to postpone a biopsy. A detailed table of assessment categories and Management recommendations is visible in Table 2.2.

Assessment	Management	Likelihood of Cancer
Category 0: Incomplete – Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison	Recall for additional imaging and/or comparison with prior examination(s)	N/A
Category 1: Negative	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 3: Probably Benign	Short-interval (6-month) follow-up or continued surveillance mammography	> 0% but ≤ 2% likelihood of malignancy
Category 4: Suspicious **Category 4A:** Low suspicion for malignancy **Category 4B:** Moderate suspicion for malignancy **Category 4C:** High suspicion for malignancy	Tissue diagnosis	> 2% but < 95% likelihood of malignancy > 2% to ≤ 10% likelihood of malignancy > 10% to ≤ 50% likelihood of malignancy > 50% to < 95% likelihood of malignancy
Category 5: Highly Suggestive of Malignancy	Tissue diagnosis	≥ 95% likelihood of malignancy
Category 6: Known Biopsy-Proven Malignancy	Surgical excision when clinically appropriate	N/A

Table 2.2: Management Recommendations and BI-RADS® Assessment Categories Concordance (American College of Radiology, 2013)

2.5 Breast Cancer Management

Since antiquity, breast cancer has been recognisable, and prevention strategies have advanced as our understanding of the disease has evolved. Hippocrates identified breast cancer as a humoral disease in 460 BC, and today, after numerous studies, it is thought to be a local disease with systemic origins. Halsted radical mastectomy was the "developed and standardised operation for breast cancer in all stages, early or late" for much of the twentieth century. According to new research on tumour biology and behaviour, less invasive surgery can be as successful as more invasive surgery. The degree of surgical resection in the breast and axilla was eventually decreased further with adjuvant therapies such as radiation and systemic therapy, ushering in a period of breast conservation. Breast cancer radiation therapy has progressed from 2D to 3D

conformal and enhanced fractional breast irradiation to reduce ordinary tissue toxicity and management time. In treating breast cancer, systemic therapy in the form of hormone therapy, chemotherapy, and biological agents is now a well-established modality. The new approach to breast cancer treatment is focused on an ever-evolving and increasingly integrated understanding of the disease's genetic, biological, biochemical, and cellular basis. The future challenge will be to use this expertise to forecast therapeutic outcomes, refine treatments, and quickly implement more innovative biologic therapeutics (Akram & Siddiqui , 2012).

2.5.1 Diagnosis of breast cancer

Breast cancer can be detected early, improving treatment options and patients' chances of survival (Jalalian et al., 2013). Breast cancer screening is vital in people who have no signs or symptoms of breast cancer to detect it early. Breast cancer treatment and early detection require a comprehensive medical history and a thorough clinical breast examination. Customizing breast cancer screening to the age and risk factors of the patient is considerable. Women that are asymptomatic but have no physical findings should be risk-stratified (Kittaneh & Glück, 2011).

2.5.2 Pathological diagnosis

When theoretically possible, histopathological confirmation should be sought whenever possible, particularly in the case of a single metastatic lesion (Cardoso et al., 2012). Usually, the pathological findings confirm a diagnosis. The two established methods for preoperative diagnosis are fine needle aspiration and a comprehensive bore needle core biopsy. There are advantages to preoperative diagnosis in women with breast abnormality. One of which for the pathologist is a decrease in time–consuming frozen sections (Weledji & Tambe, 2018).

2.5.3 Clinical Staging

The American Joint Committee on Cancer (AJCC) published a staging scheme focused on anatomic findings since its inception in 1977: tumour size (T), nodal status (N), and metastases (M). Even though physicians in practice have used a variety of biological variables to characterize the patient's condition, outcomes, and effective treatment for many years, the breast cancer staging scheme focuses on TNM classification. Estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), grade, and multigene assays are all commonly used in practice to assess prognosis and therapy. However, until recently, there was insufficient evidence to

enable biomarkers to be used in the breast cancer staging method (Giuliano, Edge & Hortobagyi, 2018).

The stage of breast cancer commonly identifies as a number on a range of 0 to IV, with stage 0 representing non-invasive tumours that remain in their original site and stage IV defining invasive cancers that have moved beyond the breast to other areas of the body (Breast Cancer.org, 2021).

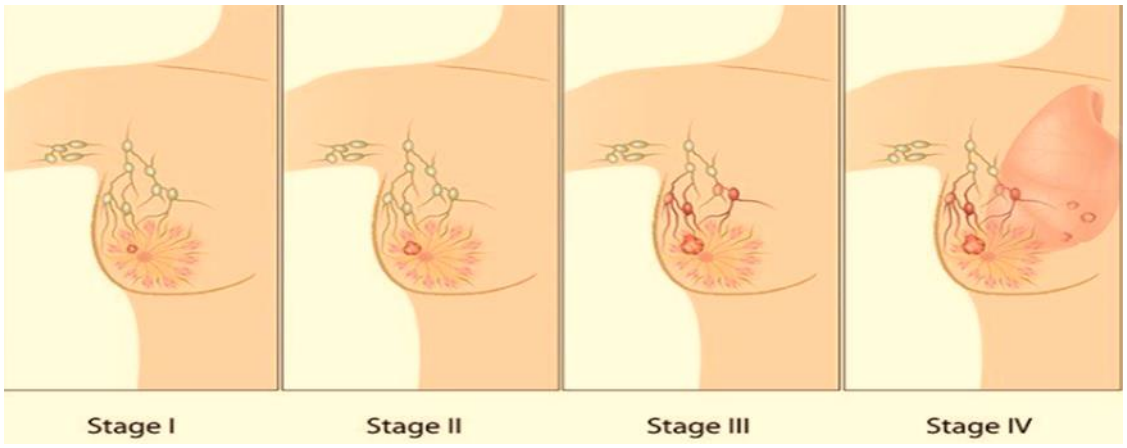


Figure 2.13: Breast cancer stages. Stage I: Cancer has become invasive and has spread beyond its original location. Stage II: cancer cells have spread to at least 1 to 3 lymph nodes under the arm and the tumour is 2 to 5 cm in size. Stage III: The malignancy has spread to 4 to 9 lymph nodes in the axilla or near the breastbone, the tumour is bigger than 5 cm or they may not even be a tumour. Stage IV: Breast cancer has spread to other parts of the body, beyond the breast and lymph nodes. Although Stage IV breast cancer is incurable, medicines can help treat it so that a woman can live for many years while managing the disease as a chronic condition (Haelle, 2021)

2.5.4 Treatment Approach

2.5.4.1 Loco regional treatment

One of the primary treatment modalities for locoregional breast cancer is surgery; the other primary modalities are radiotherapy and systemic therapy (Anderson et al., 2017). Locoregional care aims to avoid local recurrence; an IBTR rate of ≤1% per year after BCT

is a good quality measure, which individual outcome audits validate (Kaufmann et al., 2010).

Patients with just a local recurrence divide into two groups: those who had a mastectomy and those who had breast-conserving therapy. Patients who have had a mastectomy should have the local recurrence surgically resected if it is without invasive surgery and involved-field radiotherapy. In this situation, surgical resection entails a small excision of disease intending to achieve clear resection margins. After initial breast-conserving treatment, the woman should have a complete mastectomy if the disease recurs locally. Women who have local recurrences should be eligible for systemic chemotherapy or hormone therapy, just as those who have systemic recurrences should be (World Health Organization, 2006).

2.5.4.2 Systemic treatment

Targeted systemic therapies significantly impact local control, and a better understanding of how local and increasingly successful systemic therapy interact is needed (Kaufmann et al, 2010).

Systemic treatment (chemotherapy, hormone therapy, and targeted therapy) lowers the risk of cancer recurrence, and its administration happens following surgery after the pathologic stage. Chemotherapy is often provided before surgery to minimise tumour size, allowing certain previously inoperable cases to be operated on and enhancing breast conservation outcomes for borderline candidates. A clip (metal marker) is placed in the tumour bed prior to neoadjuvant treatment to ensure tumour bed localisation after chemotherapy. Even if neoadjuvant therapy has produced a complete therapeutic response and the tumour is no longer palpable in the breast and lymph nodes, surgery to remove any microscopic disease is necessary to reduce the risk of locoregional tumour recurrence (Anderson et al., 2017). Systemic therapy works as adjuvant therapy after surgery, but it can also work as a neoadjuvant therapy before surgery (Anderson et al., 2017). Shown in Figure 2.14 is the breast cancer options.

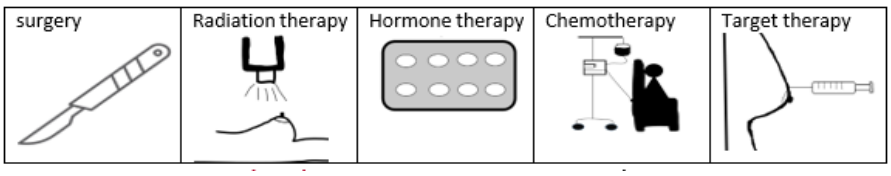


Figure 2.14: Breast cancer treatment options

2.5.4.3 Targeted therapy

With a greater understanding of the aetiology of breast cancer, molecularly targeted drugs for the treatment and prevention of breast cancer have been developed and are tested. The selective drugs such as ER modulators, tamoxifen, raloxifene, lasofoxifene and aromatase inhibitors like anastrozole, letrozole, and exemestane are studied in preclinical and clinical trials to understand the blocking of the oestrogen-activated pathways. Tamoxifen and raloxifene are a lower breast cancer risk, and promising findings of aromatase inhibitors (AIs) in breast cancer trials indicate that AIs could be even more successful in preventing ER-positive breast cancer. These drugs, however, are only effective against ER-positive breast cancer. As a result, new research focuses on finding preventive treatments for other types of breast cancer, such as HER2-positive and triple-negative breast cancer (TNBC, breast cancer that does express ER, progesterone receptor, or HER2). Anti-HER2 therapies such as trastuzumab and lapatinib used to treat HER2-positive breast cancers, and preclinical and clinical trials are also being performed to see whether these medications can also be used to prevent HER2-positive breast cancers (den Hollander et al., 2013)

Trastuzumab is the first and only FDA-approved targeted anti-cancer drug that has demonstrated a favourable response rate and outcome in patients with HER-2 positive metastatic breast cancer. Main or acquired trastuzumab resistance, on the other hand, normally develops after a period of treatment with trastuzumab and contributes to treatment resistance or tumour progression (Fang, Barekati Zhang, Liu & Zhong 2011).

2.5.4.4 Endocrine therapy

In treating oestrogen receptor-positive breast cancer, endocrine therapy is a critical component. The routine use of 5 years of adjuvant tamoxifen has increased survival rates for early breast cancer, and it has recently expanded to include aromatase inhibitors in the postmenopausal environment (Palmieri, Patten, Januszewski, Zucchini & Howell, 2014).

In 70% of breast cancers, the oestrogen receptor (ER) is the controlling transcription factor. Endocrine therapies that target the ER have proven to be one of the most effective anticancer treatments (Chang et al., 2006). Novel targeted agents are now being used in conjunction with proven endocrine therapies in the clinic to increase efficacy. Endocrine therapy is the mainstay of care for invasive breast carcinoma

patients with ER protein expression (ER) on immunohistochemistry. In the late nineteenth century, George Beatson founded this current practice (Johnston, 2015). Breast cancer patients who receive adjuvant endocrine therapy have a lower recurrence rate and a higher survival rate. Many patients never start therapy or stop it too soon. Therefore, understanding the factors that influence the initiation and maintenance of endocrine therapy may help physicians' better serve patients (Friese et al., 2013). In short, in conclusion, as stated by (Xu et al., 2020), Adjuvant endocrine therapy , such as tamoxifen and aromatase inhibitors , has shown to help the vast majority of patients.

2.5.4.5 Chemotherapy

In breast cancer, neoadjuvant chemotherapy is becoming more common, particularly for downstaging the original tumour in the breast and the metastatic axillary lymph node. Accurate assessments of neoadjuvant chemotherapy response give crucial information on the influence of systemic medicines on breast cancer biology, prognosis, and treatment options. Furthermore, pathologic complete response is a well-established and valuable surrogate predictive factor for post-treatment survival. In both clinical and basic research, evaluations of neoadjuvant chemotherapy response are critical (Wang & Mao, 2020).

2.5.4.6 Immunotherapy

The breast tumour microenvironment is immunosuppressive, and it is becoming clear that it plays a role in tumorigenesis. Researchers have harnessed the immune system with experimental immunotherapy methods, many of which have shown promise in breast cancer, thanks to a better understanding of natural and abnormal interactions between malignant and immune cells. Cancer immunotherapy refers to a group of treatments that use patients own immune systems to target and destroy tumour cells. Unlike other treatment methods, cell-based immunotherapy is a living medicine that can evolve to stay ahead of changing tumour cells and has the added advantage of being successful even when traditional cytotoxic or targeted drug therapy fails. In addition to targeting tumour cells directly, the immune system may have indirect effects by attacking tumour stroma and "resetting" the immune system to an anti-tumour surveillance status that prevents tumour outgrowth. As a result, cancer immunotherapy holds promise for cancer care and prevention (Williams et al, 2017).

2.5.4.7 Role of Surgery for breast cancer

The oldest form of oncology is surgery, dating back thousands of years. Only the courageous, desperate, or ill-advised patient underwent surgery prior to the invention of anaesthesia and antisepsis 150 years ago, though cure rates were poor, and morbidity and mortality were high(Wyld et al., 2015). Surgery is the major treatment modality for locoregional breast cancer; radiation and systemic therapy are the other primary modalities. Breast cancer surgery necessitates specialist surgical preparation and treatment management. The disease stage will determine the type of surgery, tumour characteristics, patient preferences, and neoadjuvant (preoperative) and adjuvant (postoperative) care services available. In low-resource settings, modified radical mastectomy is the chosen surgical treatment.. Breast-conserving therapy (BCT), which involves breast irradiation after surgery, becomes a viable alternative as more services become available (Anderson et al., 2017).

In addition, oncoplastic surgery (OPS) has emerged as a modern method for widening the options for breast-conserving surgery (BCS), lowering the rates of mastectomy and re-excision while preventing deformities (Clough, Kaufman, Nos, Buccimazza & Sarfati 2010).

The American Cancer Society, (2019) claims that most women with breast cancer endure surgery as part of their care and that there are several forms of breast surgery, and depending on the case, and performance depends on a variety of purposes. Check for cancer spread to underarm lymph nodes (sentinel lymph node biopsy or axillary lymph node dissection). Check lymph nodes under the arm for the spread of cancer (sentinel lymph node biopsy or axillary lymph node dissection).

The two kinds of surgery consist of: breast-conserving surgery removes only the tumour and normal breast tissue in that area Procedures such as breast-conserving surgery (American Society of Clinical Oncology, 2020) and mastectomy (Sharma et al., 2010) are the order for surgery. A lumpectomy, partial mastectomy, quadrantectomy or segmental mastectomy is an operation that removes only the malignant region of the breast. The aim is to eliminate cancer and any healthy tissue around it. The volume of breast material removed is determined by the location and size of the tumour and other factors. Mastectomy involves the whole breast, including all the breast material and possibly other surrounding tissues, is removed. Mastectomies come in a diversity of

shapes and sizes. For some women, a double mastectomy is an option for removing both breasts.

Mastectomy vs. Breast conservation

Breast-conserving therapy (BCT) is a practical first treatment choice for most women with stage I and II breast cancer. BCT gives long-term survival rates comparable to complete mastectomy while sparing the breast. BCT offers long-term survival rates comparable to total mastectomy by preserving the breast. With advancements in mammography and margin evaluation, and (primarily) because of the favourable interaction, the risk of IBTR after BCT has decreased over time. In the absence of RT, the risk of IBTR may not influence survival well. Since IBR rates greater than 10% at 5 years are linked to increased breast cancer mortality at 15 years, it is critical to pay close attention to patient selection and the technical details of the surgery and RT (Kaufmann et al., 2010).

2.5.4.8 Lymph node surgery

When breast cancer spreads to the regional lymph nodes, then . Controlling breast cancer in low-resource settings with a complete axillary dissection (removal of the tissue under the arm that involves the lymph nodes) during the definitive surgery is essential to accurately stage cancer and control it. When there is no clinical evidence of tumour activity in the axilla, a sentinel lymph node biopsy (SLNBx) is an option as more resources become available. An SLNBx is a minimally invasive procedure involving blue dye and a radioactive tracer to identify one or more lymph nodes that are most likely to be cancerous. While less intrusive than complete axillary dissection, this technique necessitates more resources and surgeon preparation. A complete surgical procedure, the full axillary lymph node dissection (ALND), may be needed if there is cancer in the lymph nodes. Since SLNBx only eliminates the first lymph nodes to which cancer may spread from the breast, it is not recommendable for more advanced or biologically aggressive cancers where severe disease may remain in the axilla (Anderson et al., 2017).

2.5.4.9 Role of radiation Therapy

Radiation therapy is a crucial component of breast cancer care. Breast cancer patients who (Fisher et al., 2002) receive irradiation have a lower risk of local disease recurrence

and have a better overall survival rate (Fisher et al, 2002). The percentage of recurrence following treatment with a combination of breast-sparing surgery and adjuvant radiation equals the percentage of recurrence after mastectomy. As a result, adjuvant radiotherapy following breast-sparing surgery is now considered essential for early-stage breast cancer care. Adjuvant radiation therapy improves local disease control and survival in patients with locally advanced disease, especially in patients with tumour metastases in the axillary lymph nodes (Owen et al., 2006).

2.5.4.10 General principles of radiation therapy

Ionising radiation is a form of physical agent used to destroy cancer cells. Ionising radiation forms electrically charged particles and deposits energy that can cause cancer death. High-energy radiation destroys cells' genetic material (deoxyribonucleic acid, DNA), preventing them from separating and proliferating further. Even though radiation affects both normal and cancer cells, radiation therapy aims to optimise the radiation dose to morbid cancer cells while diminishing exposure to normal cells neighbouring cancer cells or in the direction of radiation. Normal cells will usually rebuild themselves more quickly and maintain their normal function status than cancer cells (Baskar, Lee, Yeo & Yeoh, 2012).

2.5.4.11 Role of Systemic Therapy

Chemotherapy, endocrine therapy, and targeted treatments are systemic therapy for metastatic breast cancer (e.g., antibody-based approaches). Depending on the patient's breast cancer subtype, these agents can be used alone or in combination. As a result, phenotyping of the disease is needed, which may involve a biopsy of the metastatic site. Immunologic therapies, PARP inhibitors, PI3K inhibitors, and CDK4/6 inhibitors are among the novel therapeutic methods currently being studied in clinical trials (Liedtke & Kolberg, 2016).

2.5.4.12 Follow-up

Following primary breast cancer surgery, routine follow-up programs in specialist clinics are part of standard medical care. Follow-up appointments are arranged on a regular basis to diagnose and treat recurrence early on, as well as provide reassurance and therapeutic support to the patient. In Western countries, patients are visited for follow-up roughly 12–17 times in the first 5 years after breast cancer surgery, according to established follow-up regimens. Furthermore, the impact of follow-up on overall survival rates is debatable. Not all patients required all types of information during

routine follow-up following a breast cancer diagnosis. Individual patients' information needs, and expectations should be recognized early and integrated into follow-up routine treatment when implementing alternative follow-up schedules, to target resources and maximize the probability of positive patient outcomes (de Bock et al., 2004).

Early detection of a local or systemic recurrence does not appear to increase survival. Many breast cancer patients, on the other hand, want certainty that they are free of recurrence and that any recurrence will be identified as soon as possible (Jeevan et al., 2009).

Literature on follow-up treatment for breast cancer in developing countries seems rare. Furthermore, Agarwal et al., 2009 states that there is a need to prioritize public health education and early detection in countries where these weaknesses exist. In addition, money must be geared toward the construction of more public cancer care facilities. As these objectives are fulfilled, it is likely that breast cancer treatment in developed countries will improve significantly.

CHAPTER THREE

METHODOLOGY

The approach followed in this study is the subject of this chapter. When studying a topic in depth, this technique is very useful. The process of data collecting, and analysis is described in this chapter. At this stage multiple sources were consulted, but most importantly the surveys conducted to achieve the study objectives. A thorough description of the surveys is addressed in this chapter. The steps taken to arrive at the results stated in the following chapters are then described.

3.1 Study design

Phase 1 was a mixture of both prospective and retrospective studies. Seita, (2016) motivated this kind of study by summarizing, the timing between the exposure and the consequence is well established in this form of design. The research can be prospective, retrospective, or a combination of the two. This study used mixed-method research that incorporated constituents of qualitative and quantitative research procedures (e.g., use of qualitative and quantitative viewpoints, data collecting, analysis, inference procedures as prescribed by (Johnson, Onwuegbuzie &Turner, 2007). This style of inquiry was most suitable for addressing the research objectives of this study. Firstly, a pragmatic approach was employed to create a strong, contextualized view of underlying risk factors for breast cancer and the correlation of the calculated risk to the diagnostic outcome of the disease.

Secondly, the association of the diagnostic outcomes and recommendations related to disease management is investigated. The study has two phases; phase 1 is a quantitative study that includes questions concentrating primarily on breast cancer-related risk factors. The questions were employed to calculate the Lifetime risk of the patients and see the difficulties and association to illness outcome, followed by phase 2, a quantitative study consisting of closed-ended questions including rating scale questions. The survey investigates existing difficulties and how viable the solutions correlate to disease management – which equates to answering the objectives of this study. The pragmatic philosophy that guided this research allowed for the methodical application of an appropriate quantitative approach to achieve the study's objectives.

Study population

Phase 1; -The study population was recruited via judgemental sampling in the Health Information system (HIMS) registry, Medical Imaging departments and the manual filing cabinets at the AB May Oncology Centre. This data was collected concerning female Namibian citizens above 18 and the maximum age of 84. In addition, the study population was selected in comparison to women with breast cancer and those without breast cancer, including their lifetime risk calculated based on breast cancer risk factors in correlation to the diagnostic outcome.

Phase 2; -Participants for this phase were Six doctors, all from the AB May oncology centre, specialising in clinical oncology and gynaecological oncology. Clinicians in Namibia frequently work at multiple institutions, and a few oncology doctors in this sample worked in two separate subsystems simultaneously. The survey centred on their impressions and job experience in the exact context where the survey where given.

3.2 Inclusion criteria

For purposes of this research Namibian Women above the age of 18 attending at Medical Imaging Departments and the AB oncology centre were used as participants for the research.

Breast cancer as mentioned in the literature review is not common in women below the age of 40, hence the reason why the study used the above-mentioned age. However, the selected age of 18 was due to observations made within the (HIMS) database and breast cancer statistics at the AB May oncology centre. Females with and without breast cancer were include for purposes of comparing the Tyrer Cuzick lifetime risk calculated to the diagnostic outcome to derive its relevance or Importance. All available oncology doctors working at the AB oncology Centre in Windhoek could participate in this research.

3.3 Exclusion criteria

Men were excluded from this research as mentioned in the literature review they only account for 1 % of breast cancer patients and an insignificant amount of men attend to breast screening. Women that were not Namibian citizens were also excluded from the research. The objectives were setup for Namibian women. Women above the age of 84 were also excluded from the study as they fall into a category that is already higher than the general life

expectancy. The Tyrer Cuzick tool used to assess the risk factors also does not take this age group into consideration.

3.4 Study setting

This study was steered in Windhoek, the capital city of Namibia. The population in Windhoek is estimated at 400 000 by the city of Windhoek and the Namibian population is estimated at about 2, 540,905 people at mid-year according to the Namibian Population World meter. There are 3 private known 2-D and 3-D tomosynthesis Mammography sub departments and 1 known 2-D mammography unit. However, the state has 1 known non-functional department since dated 2017 (See limitations of breast cancer management and treatment). Medical Imaging has 2 of the 3 Private departments in Windhoek including breast MRI services, hence the choice for this study. There are 2 main oncology centres in Windhoek the AB May oncology centre at the state and the Namibian oncology centre (NOC) of which the AB May oncology centre accommodates many patients, hence the choice of collaboration for this study motivated by a few limitations from NOC.

3.5 Sample size

For phase 1 to estimate a single proportion, an epitools,(2018) epidemiological calculator was used, were a method of sample size to estimate a section or seeming prevalence with identified precision with a specified level of confidence and precision with an input of estimated proportion of 0.3, desired precision of estimate 0.05, confidence level of 0.95 of population size of 500 which gave a result of 323 for a large population sample and 197 sample size for the purpose of this research a sample size of 200 was used (Sergeant, 2018). According to the Namibian inter-censal demographic survey of a 2016 report done in 2017; there is approximately 752 619 women above the age of 15 of whom 57% are females ranging from ages 15 to 59, and 6% above the age of 60. Breast screening can be done on different age group. Women younger than 30 usually opt for breast ultrasound as it is recommended for women with dense breast or those that have not yet given birth.

However, around 7% of all breast cancers are detected in women over the age of 40, and less than 4% in women under the age of 35. Even though breast cancer is rare in young women, it is the most common cancer in women,40, accounting for 30–40% of all incident female cancers (Fredholm et al., 2009). The Namibian national cancer registry in 2017 concluded that, 549 women were diagnosed with breast cancer annually for the period 2014 to 2016.

Phase 2; the sample size was based of the convenience of the Six oncologist willing to participate. The research survey was based on the saturation of the information regarding the management of breast cancer at the AB May Oncology Centre in Windhoek, Namibia.

3.6 Sampling Technique

Phase 1; For purposes of this research Judgement sampling was used. Judgement sampling is when the researcher chooses a sample based on predominant criteria and used when sample needs to fulfil certain requirements; which in this case are women above the age of 18 with or without a high personnel lifetime risk and patient diagnosed with recent breast cancer/breast cancer onset. Judgement sampling is also selected because it is used to collect data from a system (Perla & Provost, 2012). Which for this research was the HIMS registry at Medical Imaging Departments of which somewhere patients that went for breast screening. At the AB May oncology centre patients that are still living and whose data is available and enough to complete the risk assessment forms from time of breast cancer onset, were selected for the study.

Phase 2; all oncology clinicians willing to take part were selected for this study using a convenience sampling method to explore the oncologist perspective of the management and treatment of breast cancer.

3.7 Materials and Methods

3.7.1 Data Collection

The assessment of the most common risk factors of breast cancer was included in Phase 1 of the study, a survey/risk assessment form consisting of prospective and retrospective data was collected and combined to fulfil the survey from participants that came to the Imaging department for breast screening and those patients that were newly diagnosed with breast cancer at the AB May oncology centre that recently had breast screening at Medical Imaging departments. Each participant was assigned an incognito code to preserve the participants' confidentiality. Refer to Appendix D. The information filled in the survey was then entered the Tyrer Cuzick risk assessment tool as shown in Figures 3.1 to 3.6). The different risk variables were also recorded in a Microsoft excels spread sheet. Most of the information that was needed was derived from the HIMS at the Medical Imaging departments. The risk factors

comprised in the survey were previous breast cancer diagnosis, hysterectomy, menopause, age, height, breast size, previous genetic test, weight, previous breast surgery, HRT use, contraceptive use, menarche, age at first pregnancy, number of full term pregnancies, longest time of breast feeding, previous miscarriage or abortion, race, ethnicity, family history of breast cancer and ovarian cancer, previous biopsies, previous exposure to radiation and finally BIRADS. Unfortunately, not all risk factors could be assessed due to shortcomings of incomplete and unclear data. However, risk factors that were properly recorded and documented which were used for this study were; age, height, weight, menarche, age at first pregnancy, menopause status, family history, previous genetic test, BIRADS, parity and HRT use.

The Tyrer Cuzick tool gives an estimation of the Life time risk, population risk 10 year estimated risk and the Probability risk for the BRCA1 and BRCA2 genes percentage. This risk as mentioned earlier is considered high at 20% as described in Chapter 2 (2.3.2.1 the Tyrer-Cuzick Model).

Eventually a BIRADS category was given to the patient based on the accumulative factors of the breast examination using the CAD tomosynthesis 3D mammography, MRI, Breast ultrasound and breast biopsies.

The study documented the participants risk percentage and then compared it to the participants BIRADS category risk factor. This was done to assess the most common risk factors of breast cancer.

Furthermore, the study looked at the participants' history of visitation to the department on HIMS to see if the patients followed through with the recommendations in the previous reports, which may assist in the route of managing breast cancer or to prevent the disease. To determine the most common diagnosed type of breast cancer a descriptive study of the clinical and pathological characteristics of women diagnosed with breast cancer from April 2020 to December 2020 according to the medical imaging data filing system was used; data was entered into a database and basic frequencies were calculated. Data was recorded in excel and then transferred to prism 8.

In addition, to assess and contrast the screening modalities at the Medical Imaging departments with specific reference to the Tyrer-Cuzick tool the participants were divided into

two groups a control group which consisted of participants without a breast cancer diagnoses compared to a case group consisting of patients diagnosed with breast cancer. The risk variables were calculated, and the lifetime risk recorded in an excel spread sheet for further analysis. This was done to determine the compatibility of the Tyrer Cuzick risk assessment tool amongst Namibian women.

3.8.1.1 Steps on how the Tyrer Cuzick risk assessment tool was utilised

Step 1: software was downloaded for pc computers only at http://www.ems-trials.org/riskevaluator/

Step 2: The participants code was entered as shown in Figure 3.1.

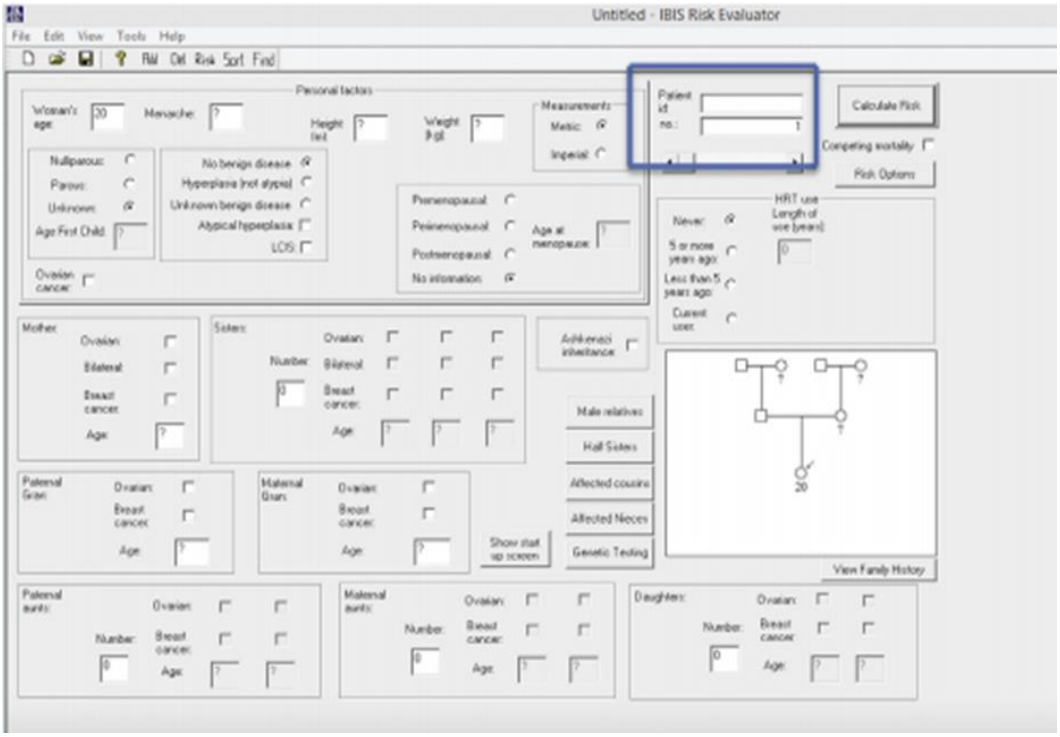


Figure 3.1: Identification number and name option (Himes D. O., 2016)

Step 3: personnel risk factors were entered such as patient age, age at menarche, height and weight measurements. The 7 metric options were used as shown in (Figure 3.2).

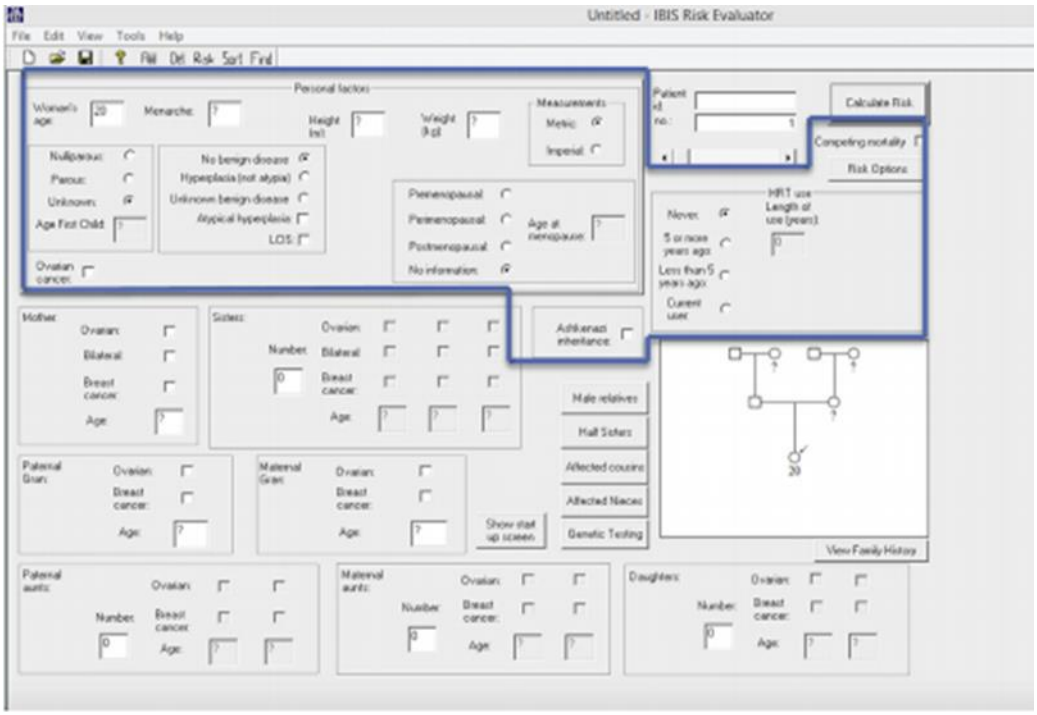


Figure 3.2: Personal factors (Himes D. O., 2016)

Parity and a history of breast disease were entered as shown in (Figures 3.3, 3.4 &3.5). No benign disease box was marked if the participant had never been diagnosed with breast abnormalities. The boxes were marked if the participant had hyperplasia, an unknown benign condition, atypical hyperplasia, lobular carcinoma in situ, or ovarian cancer. Next the participants menopausal status based on age, hormone therapy (oestrogen-only or combination (oestrogen and progesterone) menopause were entered as per instructions of the Tyrer Cuzick guide.

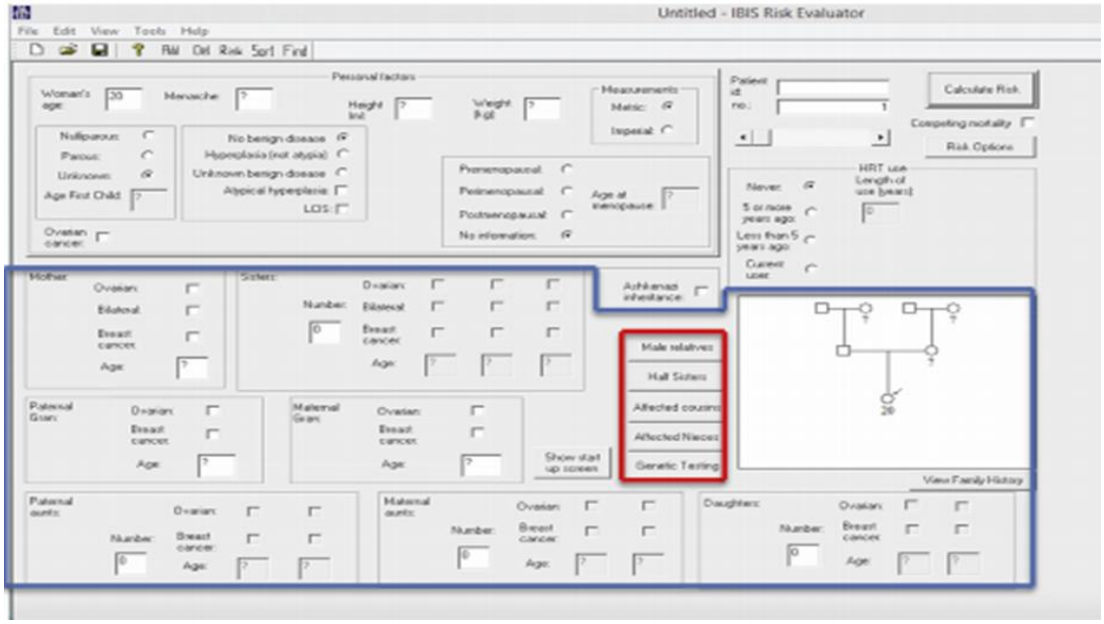


Figure 3.3: Family history; the click buttons in red should be checked last (Himes, 2016)

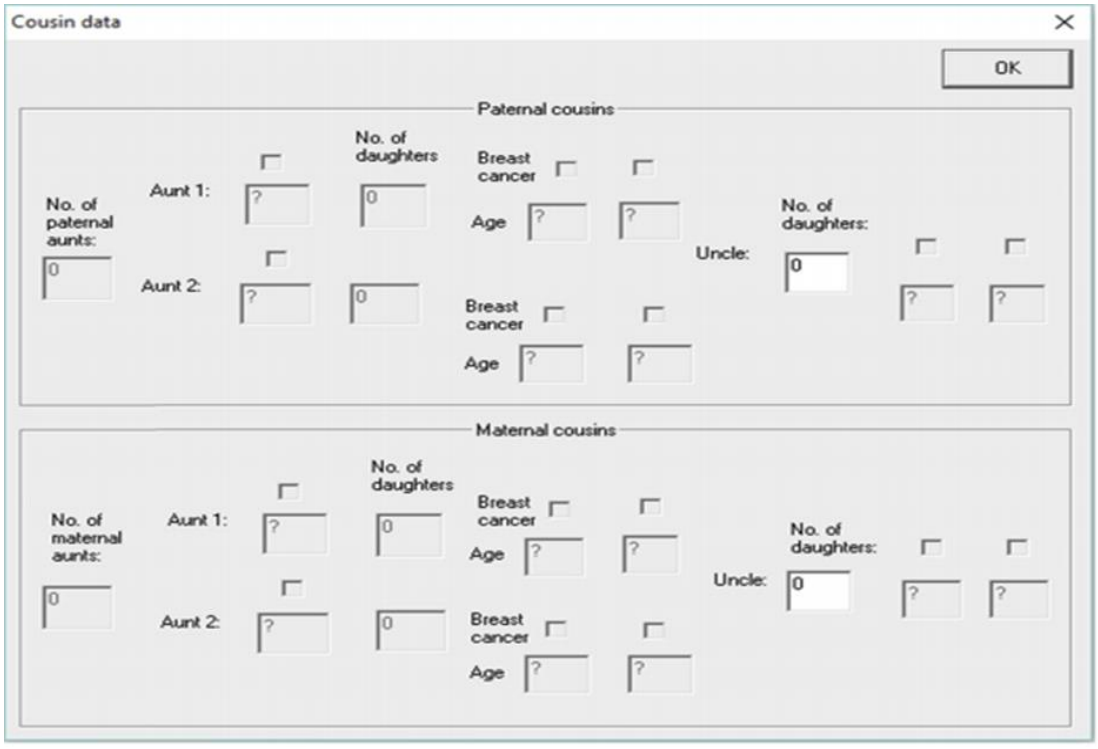


Figure 3.4: data regarding cousin with breast cancer family history (Himes D. O., 2016)

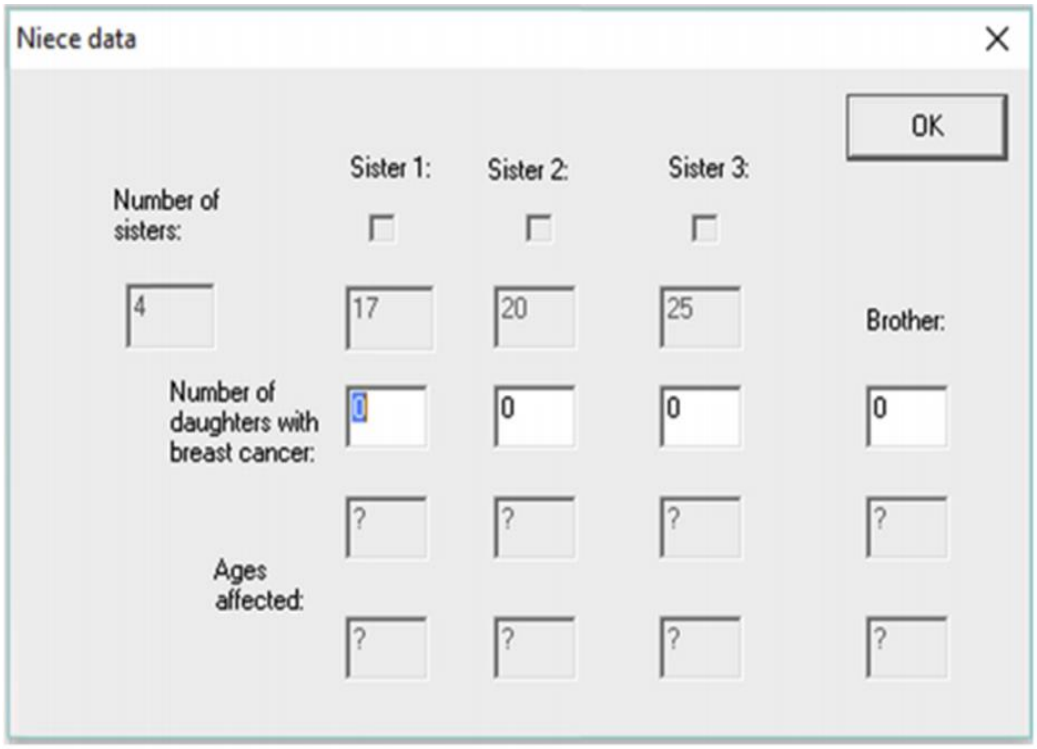


Figure 3.5: data regarding niece family history with breast cancer (Himes, 2016)

If the patient is of Ashkenazi Jewish ancestry (Eastern European Jewish), the appropriate option was checked because this community is more likely to have BRCA1 and BRCA2 gene mutations. The competing mortality box was not checked. The researcher left the box unchecked, as to use the highest possible lifetime risk.

Step 4: family history; the Tyrer-Cuzick model's most thorough sections entailed entering the family history. The overall goal of the family history section was to incorporate information about the woman's family history that may influence her risk of breast cancer. In each of these categories, the program accepted cancer history for up to 5 relatives. Because not all relatives could be included, including cancer-affected relatives were prioritized to account for the family's risk. After entering the number of first- or second-degree female relatives, the current age or the age at which the mother, sisters, grandmothers, aunts, and daughters died were entered were applicable. The boxes were marked if any of those women have had ovarian, bilateral breast cancer, or breast cancer, and the age of cancer onset rather than the present age or death age was entered. If a woman has had bilateral breast cancer or two primary

breast cancers in the same breast, the "bilateral" box was checked to account for the risk. After completion of the basic family history, the red buttons in a logical order where clicked. Shown in Figure 3.3 The male relative's button was the first to be pressed. The box that indicated the age when the consultant's brother or father was diagnosed with breast cancer was checked when necessary. After that, the button for half-sisters. Up to two paternal and two maternal half-sisters could be recorded. If they have had breast cancer, the box was checked, and the age of onset entered; if they haven't had breast cancer, their present age was entered. There is an affected cousin and nieces' option that can be checked. The model allowed for only children of two aunts and one uncle as shown in Figure 3.4 and 3.5. The last buttons are an option for genetic testing as shown in Figure 3.6, where if the patient had genetic testing the results could be entered of which none of the patients had a genetic test done before for this study.

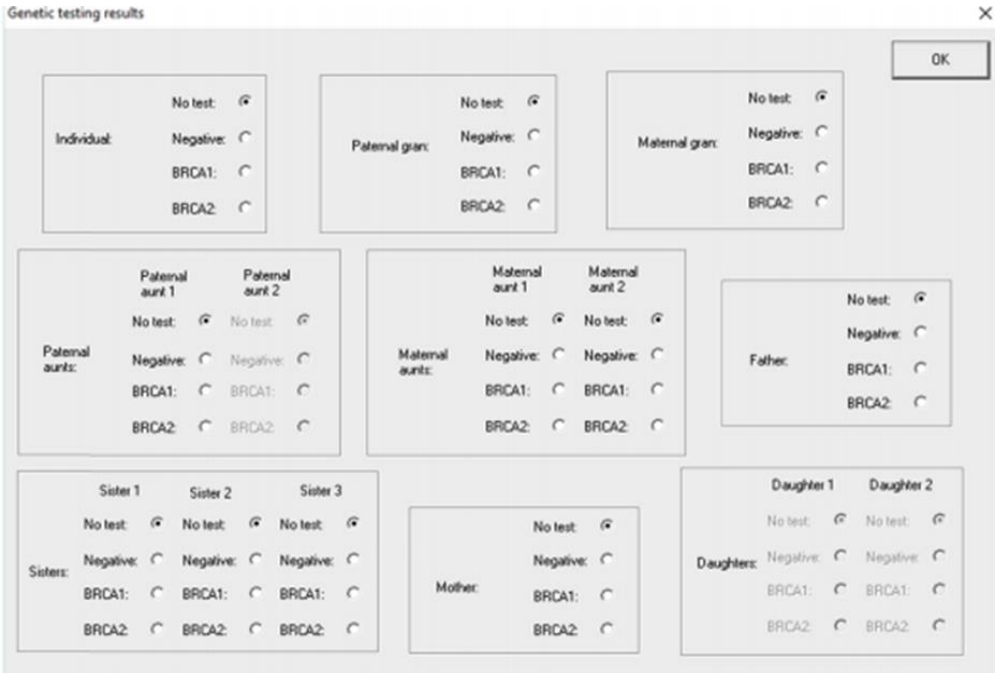


Figure 3.6: Genetic testing results (Himes D. O., 2016)

Using the Tyrer-Cuzick model had several drawbacks. Only hereditary breast and ovarian cancer (HBOC), the most common of the hereditary breast cancer syndromes, is included in this model. A mutation in the BRCA1 and BRCA2 genes causes HBOC (LeGrazie, 2011). There are numerous different hereditary breast cancer syndromes that enhance a woman's risk of breast cancer.

Finally, to assess the breast cancer management and treatment in Namibia. The study assessed the most commonly diagnosed breast cancer type through recording participant's diagnostic outcome from follow-up radiological reports and pathological reports after biopsies where performed. This was achieved to properly asses and compare the relevance of breast cancer management and treatment in correspondence to the disease outcome considering phase 2 of the study. For phase 2; Only six of the clinical oncologists were willing to participate of which all six were given a closed ended questionnaire each. Closed ended questions and rating scale were used for this study to reduce the time of the clinical oncologist on the survey. Please refer appendix D for more information on the closed ended and rating scale questions used in the survey regarding information of the management and treatment of breast cancer.

3.7.2 Data Analysis

3.7.2.1 To assess the most common risk factors of breast cancers among Namibian women visiting the Medical Imaging departments.

Information regarding the epidemiological breast cancer risk factor features were collected prospectively and partially retrospectively by filling in a modified breast cancer risk assessment form from the sample group of 200 participants. The risk assessment form included participant code, age, parity, menarche, HRT use, family history for breast and ovarian cancer, height, weight, menopausal status, participant's history of breast disease and BIRADS. Data from the surveys was used within the risk assessment tool and entered in to Excel for data cleaning and validation. The participant risk factors were divided into categories and subcategories to simplify data analysis when data was transferred to Prism 8. For this objective Prism 8 was used to achieve;

1) Comparative descriptive analysis to compare mean of the different risk factor features
2) Unpaired t-test to compare quantitative variables (e.g. parity, menarche)
3) Pearson correlation to measure the extent to which the two groups variables change together at a constant rate.

3.7.2.2 To assess and contrast the screening modalities at the Medical Imaging departments with specific reference to the Tyrer-Cuzick tool.

The Tyrer-Cuzick model uses information regarding BRCA1/2 mutation carrier status as well as other risk factors such as age at menarche, parity, age at first childbirth, age at menopause, atypical hyperplasia, lobular carcinoma in situ, height, and BMI to estimate the risk of breast cancer. Less than 15% is considered average risk. Between 15-19% is considered intermediate risk and Greater than 20% is considered high risk. The Tyrer-Cuzick model's risk factors were compiled for each female and entered into the model by means of a computer tool developed for the IBIS risk evaluator (v 7.02) breast cancer prevention research. This study used the reported data to recreate the most comprehensive pedigree feasible for women reporting a family history to capture the arrangement of breast and ovarian cancer indicated by the participant. The Tyrer-Cuzick model was used to forecast each woman's likelihood of acquiring invasive breast cancer within the next 10 years and 1 year, using the patient's age at the time of the benign breast biopsy as the age of risk assessment. The lifetime risk data entered for every participant was validated by using excel validation tool. As well as verified by the Healthcare practitioners who availed data of participants records as relevant to the study. Lifetime risk for women diagnosed with breast cancer and those without breast cancer were transferred to prism 8. And statistical analysis was performed using prism 8 to achieve; Descriptive statistics to compare the control and case group within the sample size of 200 participants.

3.7.2.3 To assess the breast cancer management and treatment in Namibia

The most common diagnosed type of breast cancer was derived from the sample size used within this study to compare the breast cancer diagnosis to the treatment outcome. As the study seeks to investigate what are the common treatments and management methods and why they are used. Recent treatment and management methods were sought using a survey presented to the oncologist and medical officers present at the time of the data collection for the study at the AB oncology centre. Survey consisted of quantitative closed ended and rating scale questions to better understand the treatment and management of the outcome of breast disease. Data collected was recorded in Excel, the survey questions were categorized into different themes and subthemes (e.g. Availability and Importance of breast disease), the participants' answers were analysed. For Yes, No, Never and Sometime answers codes were

given 0,1,2,3 respectively. A rating scale was used for the scale type of answers with the range of 0 to 10 with 0 being no exertion and 10 being maximum effort.

3.8 Reliability

The instrument used to assess the breast cancer risk factors (Tyrer-Cuzick) is most common and acclaimed as one of the best breast cancer risk assessment tools.

3.9 Ethical Considerations

Ethical clearance was sought from the Ministry of Health and Social Services (MOHSS) ethics committee and the Namibian University of Science and Technology (NUST) higher degree committee to progress with the mentioned study. The certificate 17/3/3 MSK was obtained and dated 17 December 2019. Permission from the respective Medical Imaging departments was sought to carry out the study in the different departments around Namibia with regards to the diagnostic reports, permission was granted in January 2020. Refer to appendix B.

Participants' identities were kept confidential. Participation of women in the study was entirely voluntary and were kept anonymous during the research. The researcher focused on caring, preventing harm and protecting the dignity of the participants and their information in this research. Consent was sought from Participants for risk assessment surveys. Refer to appendix D and E.

Permission was sought from the Health department such as the AB May Centre in charge to access patients' records and gather general information about the patient that could be useful to the researcher in terms of meeting the objectives of the research. Refer to annexure C. Collected data will be protected by using a strong password on electronic data and any paper-based data will be locked away in a safe Cabinet by the researcher, instead of using the patient's real identity, a code number was used. Only the researcher and the Supervisors will have access to the data collected, after the study is completed, the data collected will be destroyed or given over to the Imaging Departments involved to raise and create further options for new research.

CHAPTER FOUR

RESULTS

4.1 Phase 1; Epidemiological, demographic and reproductive breast cancer risk factor

For the most common risk factors of breast cancers amongst Namibian women visiting the Medical Imaging Departments 200 women were included in the study and were divided into two populations: a population of 100 women with breast cancer (Case group) and 100 without breast cancer (Control group). Results of the general setting of the population are presented in Tables 4.1. The BMI, Height of participants, age at first pregnancy, age at menarche, menopausal status and HRT Status were similar for both case and control groups. Although the means of both case and control groups were similar, it is worth noticing that 5 participants (2.5%) of the case group were below 30 years.

The mean menarche age was similar for the two groups with no statistical significance *p*-value 0.157(Table 4.2). Three women (3%) of the control group have their menarche below 12 years old while all the 100 case participants (100%) have their menarche above 12 years.

Moreover, only 9 participants (7 controls and 2 cases) from the overall study population have used HRT at the time when the research was conducted. For the distribution of HRT 1% of the overall population that was on HRT was diagnosed with breast cancer, 95.5% of the overall population never used HRT and 3.5% of the overall population who used HRT were from the control group patients without breast cancer at the time of study (Table 4.2). The Fischer's exact t-test resulted in a 0.1883 *p*-value for the mean HRT use for both groups, and there was a statistically significant variance of <0. 0001 *p*-value as shown in (Table 4.2 and Table 4.3).

A total of 83 (46 cases versus 37 controls) and 117 (54 cases versus 63 controls) participants of the study were respectively pre- and post-menopausal women. Moreover, no statistical difference amongst the two groups was observed (*p*-value 0.1883 Table 4.2).

The reproductive risk factors associate to breast cancer by age groups are presented in Table 4.2. The frequency of women at older age with 1st full term pregnancy of women below and above 30 years are respectively similar for both control and case groups (78 Vs 79 and 16 Vs 14). (Table 4.2). Furthermore, the study found that both groups had similar number of women that were nulliparous and 78.5% of the overall population were multiparous (Table 4.2). As shown in Table 4.2, there was a controversial result found in patients with a family history of breast cancer within the control group as compared to the case group with a statistically significant amount of 28(68%) vs 13(31%); *p*= 0.0136). Family history risk was higher or equal in all the age subcategories of the control compared to the case group.

Table 4.3 shows a significant t-test p-value of 0.0084 for family history and a significant variance F-test p-value for HRT use <0.0001, Family history 0.0044 and Height0.0097. There is relationship between Height, Family History, HRT and breast cancer among Namibian women attending Medical Imaging.

Table 4.1: Descriptive epidemiological and demographic characteristics

Demographic and epidemiological features			
	Case group	**Control group**	**P value**
Characteristics	n=100(50%) of N	n=100(50%) of N	
Age group (mean ± Std)	50.95 ±12.39 ±	50.82 ±10.25	0.317
>65 50-65 40-49 30-39 <30	14(7) 35(17.5) 34(17) 12(6) 5(2.5)	12(6) 37(18.5) 38(19) 13(6.5) 0(0)	
Height in meters(m)	1.616 m ± 0.067	1.625 ± 0.087	0.423
BMI (Kg/m2)	28.40 ± 5.82	29.66 ± 5.92	0.131
Age at menarche (mean ± SD years)	14.93 (1.86)	14.54(2.02)	0.157
Age at 1st pregnancy	21.35 ± 7.746	22.85 ± 8.337	0.189
Menopausal status (%)	Percentage is within brackets		
Yes No	54(27) 46(23)	63(31.5) 37(18.5)	0.993
Family History of BC or OC			
Yes No	13(6.5) 87(43.5)	28(14) 72(36)	0.675
HRT Status			

Yes No	2(1) 98(49)	7(3.5) 93(46.5)	0.699

Table 4.2: Fischer's exact test epidemiological and demographic characteristics specific to age groups

Characteristics	**Age group<30**		**Age group 30-39**		**Age group 40-49**		**Age group 50-65**		**Age group >65**		**Overall series**	
	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case	Control	Case
Menarche	0	5	13	12	38	34	37	35	12	14	100	100
<12	0	0	0	0	2	0	0	0	1	0	3	0
≥12	0	5	13	12	36	34	37	35	11	14	97	100
***p*-value**	**>0.9999**		**>0.9999**		**0.4945**		**>0.9999**		**0.125**		**0.2462**	
Menopause	0	0	1	0	17	7	34	32	11	15	63	54
<55	0	0	1	0	17	7	11	11	0	0	29	18
≥55	0	0	0	0	0	0	23	21	11	15	34	36
***p*-value**			**>0.9999**		**>0.9999**		**>0.9999**		**>0.9999**		**0.1883**	
HRT												
Yes	0	0	1	0	3	1	3	0	0	1	7	2
No	0	5	12	12	35	33	34	35	12	13	93	98
***p*-value**	**>0.9999**		**>0.9999**		**0.6167**		**0.24**		**>0.9999**		**0.1697**	
Family Hx	0	5	13	12	38	34	37	35	12	14	100	100
Yes	0	0	6	1	9	5	9	4	4	3	28	13
No	0	5	7	11	29	29	28	31	8	11	72	87
***p*-value**	**>0.9999**		**0.073**		**0.385**		**0.2224**		**0.6652**		**0.0136 (s)**	
Previous breast /Ovarian CA												
Yes	0	0	1	0	0	1	0	0	0	0	1	1
No	0	5	12	11	38	33	37	35	12	14	99	99
***p*-value**											**>0.9999**	
Age at 1st full term pregnancy	0	5	13	12	38	34	37	35	12	14	100	100
None	0	2	0	2	5	0	0	1	1	2	6	7
<30	0	3	10	7	26	27	31	32	11	10	78	79
≥30	0	0	3	3	7	7	6	2	0	2	16	14
***p*-value**	**>0.9999**		**>0.9999**		**>0.9999**		**0.2637**		**0.4783**		**0.8425**	

Table: 4.3: T-test and F-test analysis for the epidemiological and demographic risk factors for case and control group overall population sample

characteristics	**t-test *p*-value**	**T, df**	**Mean (Std deviation)**		**95% CI**	**F-test *p*-value**	**R squared**
			case	control			
Age	0.9356 (ns)	t=0.08084, df=198	50.95(12.4)	50.82(10.3)	-3.301 to 3.041	0.0616 (ns)	3.30E-02
BMI	0.1308(ns)	t=1.517, df=198	28.4(5.82)	29.7(5.91)	-0.3772 to 2.895	0.8713 (ns)	0.01150
Height	0.4225(ns)	t=0.8037, df=198	1.62 (0.0668)	1.62 (0.0868)	-0.01279 to 0.03039	0.0097 (S)	0.003252
Menarche Age	0.1568(ns)	t=1.421, df=198	14.9 (1.86)	14.5 (2.02)	-0.9311 to 0.1511	0.4210 (ns)	0.01010
Age at 1st pregnancy	0.1890(ns)	t=1.318, df=198	21.4 (7.75)	22.9(8.34)	-0.7442 to 3.744	0.4662 (ns)	0.008698
Family Hx	0.0084(S)	t=2.660, df=198	1.87(0.338)	1.72(0.451)	-0.2612 to -0.03882	0.0044 (S)	0.03451
Menopause	0.1984 (ns)	t=1.291,df=198	1.46 (0.501)	1.37 (0.485)	-0.2275 to 0.04753	0.7524 (ns)	0.008341
HRT	0.0889 (ns)	T=1.709, df=198	1.98 (0.141)	1.93 (0.256)	-0.1077 to 0.007681	<0.0001 (s)	0.01454

The likelihood of participants being diagnosed with breast cancer due to the exposure of specific risk factors of breast cancer according to the standards is presented with Odd ratios (OR) and Relative risk (RR) at a 95% Confidence Interval level for the given p-value (Table 4.4). The heights of women comprise between 1.59 to 1.62 m had a significant p-value of <0.0001. Family history had a significant p-value of 0.0136.

Table 4.4: Odd Ratios and relative risk for selected breast cancer risk factors within selected categories using the Fisher's exact test

Characteristics and parameters	RR	OR	95% CI (RR)	*P*-value
Age ≥40	0.8616	0.7295	0.6354 to 1.279	0.5530
Height 1.59 -1.62 (M)	1.820	4.279	1.403 to 2.325	<0.0001
BMI >25 overweight	0.9499	0.9012	0.7123 to 1.323	0.8720
Menarche Age <12 Early	0.5792	0.3952	0.2932 to 0.9923	0.0744
1st Pregnancy Age <30 Early parity	1.164	1.332	0.7701 to 2.011	0.6570
Family Hx	0.5795	0.3842	0.3511 to 0.8851	0.0136
Menopause ≥55	1.281	1.571	0.8565 to 1.984	0.2621
HRT Used	0.4331	0.2711	0.1225 to 1.085	0.1697
The selected categories for the different characteristics were based of high-risk factors recommendations for breast cancer. Age 40 is the recommended baseline for mammography breast screening. The height was selected regarding the average range in meters amongst Namibian women from the overall study population groups. (CI); confidence interval. (ns); not significant, (s); significant, (RR) Relative risk, (OR) Odd Ratio. Significant threshold p-value <0.05.				

The mean height was statistically not significant, but similar within the two groups however Figure 4.1 shows an interesting inverse proportionality. The highest number recorded in height is between 159cm and 162cm amongst the case study group also observed as the lowest number recorded in height for the control group. The range between the two groups spreads from as little as 5% all the way to 25%. More so there is a remarkable statistically significant variance in the height category 159-162 cm with a p-value of 0. 0097, (1. 62m (0. 0668) and 1. 62m (0.0868)) for case group and control group respectively Table 4.3).

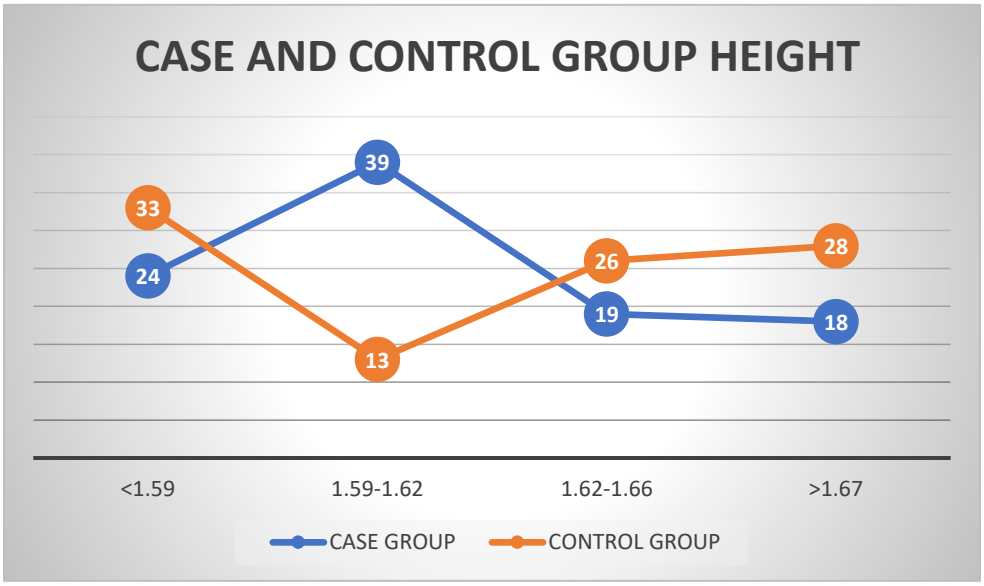


Figure 4.1: Height as a commonly significant risk factor for Namibian women

The BIRADS distribution of the 200 mammography examinations during 2020 in the Medical Imaging departments is shown in Table 4.5. As the BIRADS 5th edition states that the reporting radiologist will categorise a BIRADS 0 if the findings need further evaluation, such as a breast ultrasound or an MRI. Categories 4 and 5 generally mean that the radiologist would need to recommend for further histopathological evaluation, such as a stereotactic biopsy, core biopsy and an FNA. The analysis of the mammogram finding is depended on the decision made by the radiologist for BIRADS 4 and 5 of the likely would of breast cancer. Of the overall population group, BI-RADS 5 constituted 3.5% of cases (7 cases), and BI-RADS 4 49% (99 cases). BI-RADS 4 was considered a whole without the subdivision of 4a, 4b and 4c.

Table 4.5: BI-RADS Category risk factor for Namibian women, the number of mammograms and their distribution percentages within the population sample size

In the Private Medical Imaging Department facility, mammography is distributed into the BIRADS categories.		
BIRADS categories	No. of mammograms	% of mammograms
Category 6	0	0%
Category 5	7	3.5%
Category 4	99	49.5%
Category 3	37	18.5%
Category 2	54	27%
Category 1	0	0%
Category 0	3	1.5%
Total	200	100%

Table 4.6 shows the frequency distribution of positive predictive values (PPV) accounting to the BI-RADS categories. Of the 200 participants 7 were assumed a BI-RADS 5 diagnoses of which all 7 were diagnosed with breast cancer; this result indicated 100% accurate diagnostic assumption. BI-RADS 4 category consisted of 99 participants of which only 86 where diagnosed with breast cancer, this result indicated 86.8% accurate diagnostic assumption for breast cancer. Surprisingly all the 3 participants with BI-RADS 0 where diagnosed with breast cancer.

Table 4.6: Frequency distribution of Positive predictive values (PPV) accounting to BI-RADS categories

BIRADS categories	Total no of mammograms	Total no of BC	PPV
Category 6	0	0	0%
Category 5	7	7	100%
Category 4	99	86	86.87%
Category 3	37	4	10.80%
Category 2	54	0	0%
Category 1	0	0	0%
Category 0	3	3	100%
Total:	200	100	50%

BC; Breast cancer.

Figure 4.2 shows false positives, false negatives, true positives and true negatives BI-RADS limitations. A false-positive result screening mammogram with a BI-RADS score of 0,3, 4, or 5 require additional diagnostic tests (results within the next three months) and for which a diagnosis of invasive breast cancer or ductal carcinoma in situ was not made in the immediate recall assessment for the false- positive which is 32%. A True positive, directs existence of disease and the disease is extant the results for this was 68%. True negative indicates assumption of no presence of disease with no actual disease detected, for this Sample all the predicted BIRADS categories of 1 and 2 which indicate probably benign findings had a 100% accurate prediction of no presence of disease. False negative is the assumption that disease is not present, and the results are negative for the presence of disease, the results indicated a 100% prediction for this as well.

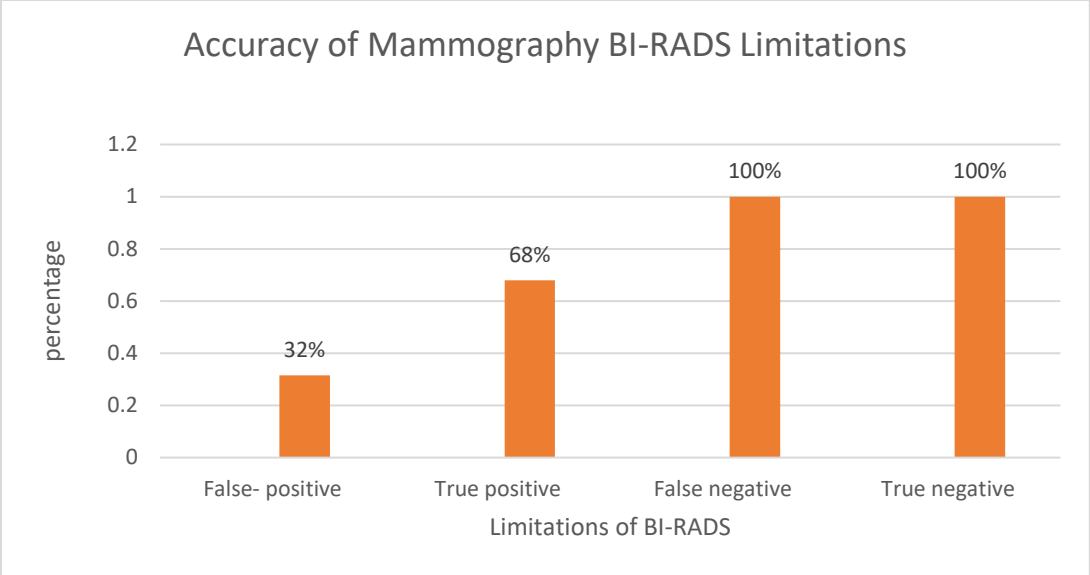


Figure 4.2: Distribution of BIRADS limitations. In summary False positives are benign findings that look malignant, false negatives are malignant findings that look benign, true positives are malignant findings that look malignant and true negatives are benign findings that look benign

4.2 Phase 1; Tyrer Cuzick breast cancer risk assessment tool compatibility for Namibian women

The 200 Participant women were divided into a 100 women of the case group diagnosed with breast cancer and 100 of the control group not diagnosed with breast cancer. Participants were selected randomly if they met full criteria established in the study. The Tyrer-Cuzick score assesses the chance of a person developing breast cancer due to specific gene alterations. The score aids doctors in determining individual's risk of acquiring breast cancer and may aid in making screening recommendations. The Tyrer Cuzick tool calculates the lifetime risk score by using the breast cancer risks as mentioned in chapter three. The lifetime risks were divided into 5 % categories for both groups. Category 0-5 being the lowest category and >20 being the highest category shown in Figure 4.3. The Tyrer Cuzick model predicted none of the women as high risk (>20%) amongst those diagnosed with breast cancer. However, among the women diagnosed with breast cancer, 5% of the participants are classified into the 16-20% lifetime risk range. In addition, among participants without breast cancer, (8%) were predicted as a highest lifetime risk for breast cancer and 11% of the participants are classified into the 16-20% lifetime risk range 44% of the women were diagnosed with invasive breast cancer of the complete

sample size with the mean life-time risk of 9%. The Tyrer Cuzick model predicted all of women as low risk amongst those diagnosed with breast cancer. Amongst the participants without breast cancer (92%) were predicted as a low risk for breast cancer. The highest recorded risk for breast cancer participants was (18%) whereby the highest recorded for the control group was (32%). The mean lifetime risk for overall sample size of 100 breast cancer participants (8.6%) with SD (3.3%). The mean lifetime risk for overall sample size of 100 control group participants (11.2%) with SD (5.7%).

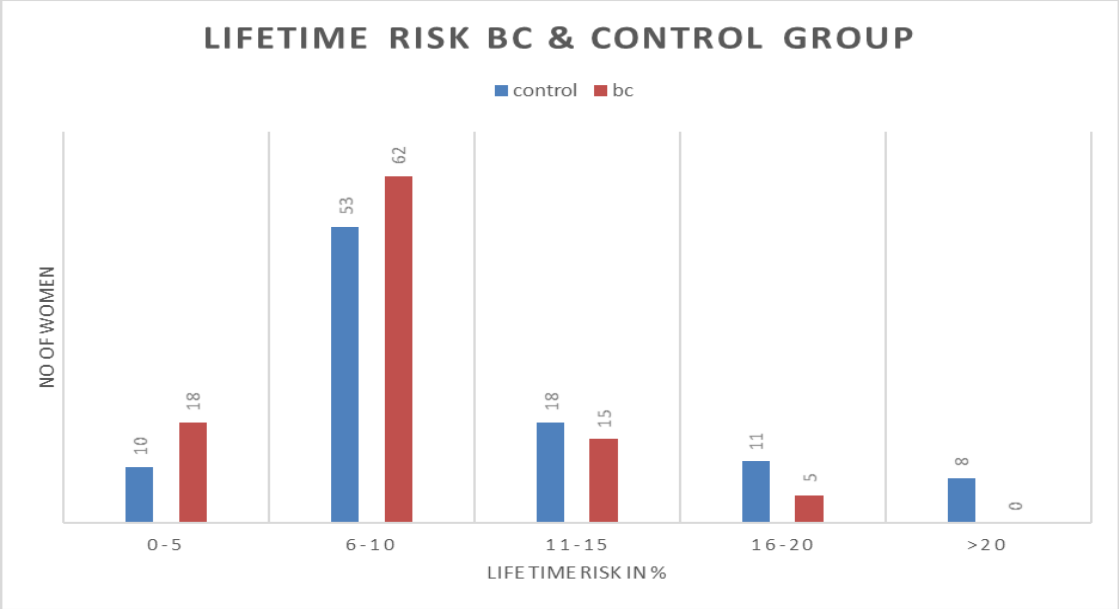


Figure 4.3: Risk prediction by the Tyrer Cuzick model for participants with breast cancer and the control group by 10- year breast cancer prediction in the first year.

Of the 200 participants, 106 (53%) of women had a breast biopsy. With 93 (88%) of the women diagnosed with breast cancer of the overall percentage of women that got a biopsy and 13(12%) of females not diagnosed with breast cancer. In the therapy of suspected breast lesions found by screening or during the examination of clinical abnormalities, percutaneous image-guided needle biopsy is critical. The mean lifetime risk for case group amongst those participants that received a biopsy were 8.79% with a ± standard deviation of 3.3% and the mean lifetime risk for the control group was 10.9% with a ± standard deviation of 5.7% when analysed using prism 8 descriptive statistics Table 4.7.

Table 4.7 Distribution of lifetime risk for patients that had a biopsy within the sample size in both groups compared to the overall sample size of participants

Categories of lifetime risk %	Overall participants (sample size 200)		Overall biopsied participants sample (106)	
	Case group	Control group	Case group	Control group
(0-5)	18	10	14	2
(6-10)	62	53	60	4
(11-15)	15	18	14	4
(16-20)	5	11	5	2
(>20)	0	8	0	1
Total participants	100	100	93	13
The Mean lifetime risk %	8.7%	11.1%	8.8%	10.9
Std Deviation	3.3	5.7	3.3	5.7

4.3 Phase 2: Breast cancer treatment and management

The most commonly diagnosed type of breast cancer was derived from the total number of 100 case group participants within the sample size of 200 overall participants. Shown in Figure 4.4 is the different kinds of histopathological breast cancer diagnosis. Of all cases within the sample size 43% of women were diagnosed with Invasive ductal carcinoma as the most commonly diagnosed type of breast cancer. Overall ductal carcinoma cases are the most in this study

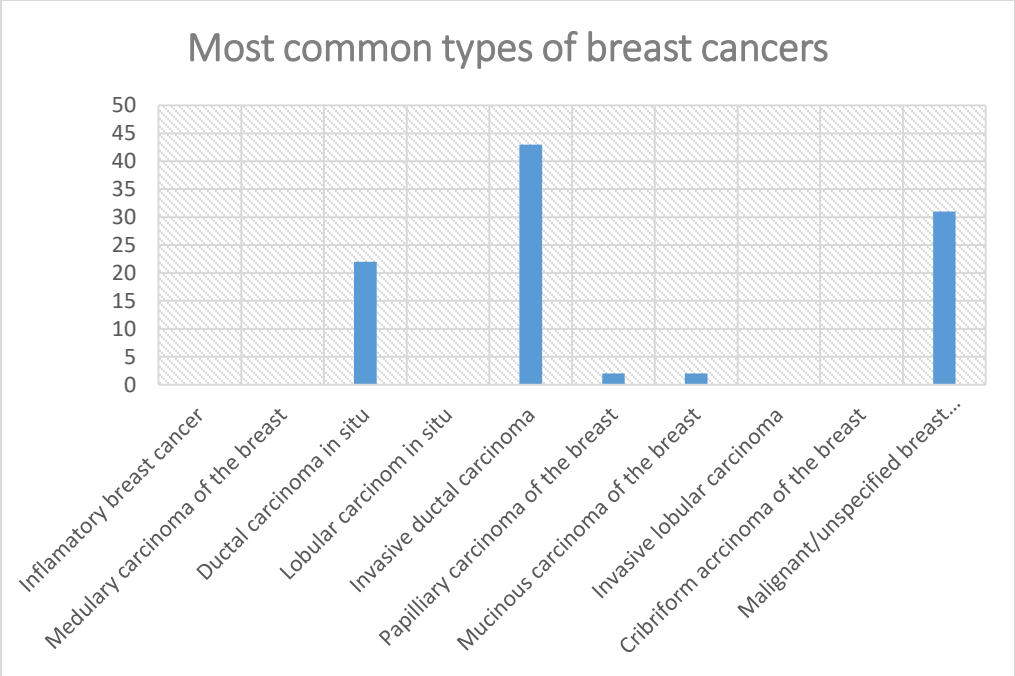


Figure 4.4: Most common types of breast cancer for Namibian women being treated at the AB May oncology centre 2020

Breast cancer management and treatment data was recorded using multiple response questions from the oncologist and clinicians at the AB May oncology centre. The multiple question responses were analysed using a constant comparative technique and thematic analysis. The overall general themes were six: commonly used treatment methods, treatment options available, treatment challenges for oncologist, recommendations for improving treatment, patient's adherence and availability and importance of breast disease management.

Table 4.8 shows the themes of the oncologist at the AB May oncology centre. The most commonly used and available treatment methods are chemotherapy, radiation therapy, hormonal therapy, targeted therapy, surgery, immunotherapy and some other methods available not mentioned but used scarcely. Challenges experienced by the oncologist for management and treatment of disease as indicated by the results is insufficient resources at the most with 100% agreement of all the oncologist that participated, intense workload and patients showing with advanced disease 83.3% agreement and a lack proper facility like digital systems. The oncologist recommended mostly educating and creating awareness of breast cancer, then at the same level introducing a digital system, employing more oncologist and

oncology health care workers and finally to increase resources and facilities to introduce integrated health systems.

The second main theme is patient's adherence as shown in Table 4.9. Fortunately, according to the oncologist at the time of the study it indicated that patients follow their given regiments and show up for follow-up consultations. Patients present with advance disease and understand their treatments options above average.

The last main theme is the availability of treatment options and recommendations for management of breast disease shown in Table 4.10. At the time of the study as indicated by the results there was treatment policy available at The AB May centre. Fortunately, there is a high availability for supportive care for survivors of breast cancer as well as a survivorships plan. However, there is no primary source for breast cancer gene testing in Namibia, even though there are measures in place to get results from elsewhere, the availability of gene testing and chemoprevention methods are very low as indicated by the results. The oncologist exclusively recommended implementation and awareness of breast cancer gene testing, breast cancer risk factor education and proper recording and record keeping of the breast cancer risk factors. Sharing of patients' information with the surgeons was highly recommended. Patients being traced for follow-up consultations and enough treatment options were recommended above average.

Table 4.8: The degree of agreement of oncologist toward a given theme and subtheme. Coding: Number 0; Yes and 1; No

		particpant 1	particpant 2	particpant 3	particpant 4	particpant 5	particpant 6	number of (yes)	number of (no)	Degree of agreement (%)
Themes	**Subthemes**									
commonly used treatment methods	surgery	1	0	0	0	0	1	4	2	66.60%
	radiation therapy	0	0	0	0	0	1	5	1	83.30%
	hormone therapy	0	0	0	0	0	1	5	1	83.30%
	targeted therapy	0	0	0	0	0	1	5	1	83.30%
	chemotherapy	0	0	0	0	0	0	6	0	100%
	imunotherapy	0	1	0	1	1	1	2	4	33.30%
	other	1	1	1	0	1	1	1	5	16.70%
treatment options avaialbe	surgery	1	0	0	0	0	0	5	1	83.30%
	radiation therapy	0	0	0	0	0	0	6	0	100%
	hormone therapy	0	0	0	0	0	0	6	0	100%
	targeted therapy	0	0	0	0	0	1	5	1	83.30%
	chemotherapy	0	0	0	0	0	0	6	0	100%
	imunotherapy	0	1	0	1	1	1	2	4	33.30%
	other	1	1	1	0	1	1	1	5	16.70%
treatment challenges for oncologist	lack of facilities	0	1	0	0	1	1	3	3	50.00%
	intense workload	0	0	0	0	0	1	5	1	83.30%
	digital facilities	0	0	1	1	0	0	3	3	50.00%
	no show patient	1	0	0	1	1	1	2	4	33.30%
	pts not understanding treatment	0	1	0	1	1	1	2	4	33.30%
	pts time management	1	1	0	0	1	1	2	4	33.30%
	show with advance disease	0	0	0	0	1	0	5	1	83.30%
	insufficient resources	0	0	0	0	0	0	6	0	100.00%
	cooperation referal drs	0	1	1	1	1	0	2	4	33.30%
	other	1	1	0	1	1	1	1	5	16.70%
	none of the above	1	1	1	1	1	1	0	6	0.00%
recommendations for treatment	increase resources	0	0	0	0	1	1	4	2	66.70%
	educate and create awareness	0	0	0	0	0	0	6	0	100.00%
	introduce digital facilities	0	0	0	1	0	0	5	1	83.30%
	intergrated systems	0	1	0	0	1	0	4	2	66.70%
	digital filing	0	1	0	1	0	0	4	2	66.70%
	more oncologist	0	0	0	0	0	1	5	1	83.30%
	more oncology health workers	0	0	0	0	0	1	5	1	83.30%
	increase facilities	0	1	0	0	0	1	4	2	66.70%

Table 4.9: Patient adherence theme scaling according to Medical oncology clinicians' perception of experience

Scaling for Theme: patients adherance	Partcipants 1	Partcipants 2	Partcipants 3	Partcipants 4	Partcipants 5	Partcipants 6	overall scale no	Total number scale	(%)percentage
Scale from 1-10									
Subtheme									
Patients understanding treatment option	6	9	5.5	5	6	8	39.5	60	65.83
Patients presenting with advance disease	7	4	6.5	5	10	7	39.5	60	65.83
Patients showing for follow-up	9	8.5	8.5	8	8	8	50	60	83.33
Patients follow regiments	10	10	8.5	8	8	7	51.5	60	85.83

Table 4.10: Treatment availability and recommendations, the experience and perception of clinical oncologist

Theme for availability and importance	particpant 1	particpant 2	particpant 3	particpant 4	particpant 5	particpant 6	yes(%)	no(%)	never(%)	sometimes(%)
management of Breast desease										
Subtheme										
availability of treatment policy	0	0	0	0	0	0	100	0	0	0
availability of gene testing	1	1	1	0	1	0	33.3	66.7	0	0
recommend gene testing	0	0	0	0	0	0	100	0	0	0
awareness of gene testing	1	0	0	0	0	0	83.3	16.7	0	0
availibility of chemoprevention	1	1	0	1	0	1	33.3	66.7	0	0
sufficient treatment options	3	1	0	0	0	0	66.7	16.7	0	16.7
BC risk factor knowledge important	0	0	0	0	0	0	100	0	0	0
recording risk factors important	0	0	0	0	0	0	100	0	0	0
availibility of survivorship plan	1	0	0	0	0	0	83.3	16.7	0	0
sharing patient information with surgeons	3	0	0	0	0	0	83.3	0	0	16.7
availability supportive care for survivors	0	0	0	0	0	0	100	0	0	0
patients traceable for recall/follow-up	3	0	0	3	0	0	66.7	0	0	33.3
coding : yes;0, no; 1, never; 2, sometimes;3										

CHAPTER FIVE

DISCUSSION

This chapter is divided into three main sections to respectively discuss the objectives of the study. The first section will discuss the epidemiological and demographic risk factors of breast cancer. The second section will discuss the Tyrer-Cuzick life-time risk compatibility assessment and the final section will be focused on the breast cancer management and treatment from the perspective of the Clinical Oncologist at the AB May Centre.

5.1 Phase 1; Epidemiological and demographic risk factors of breast cancer

Age: Although the statistical significance of breast cancer for age ≥40 years is not significant when doing a chi-square test to compare the case and control groups, the overall ages for the two populations are significant. The results indicated that women between the subgroup ages 40-65 years correspond positively with breast cancer risk. These results could also be altered or determined by the odds of the age groups of women recommended going for breast screening. Being a woman and growing older are the two main risk factors for breast cancer, with most cases occurring in women over 50 (DeSantis et al., 2014). The results of this study are in line with that conclusion. According to the American Cancer Society Trusted Source, people at average risk for breast cancer should start getting annual mammograms at 40. Those aged 45–54 should have a mammogram every year, with the option to transition to every other year after they reach the age of 55. Other personal characteristics may also influence the frequency of testing.

BMI: a study done by (Crispo et al., 2015) a study done by (Crispo et al., 2015) demonstrated that obesity has a role in women's' breast cancer prognosis regardless of diagnosis mode, highlighting the potential influence of high body weight on breast cancer prognosis. Studies have shown an association with breast cancer, with increased BMI being a protective factor amongst premenopausal women (Guo et al., 2016; Liu et al., 2018). On the contrary, another study concluded that in both the pre-and postmenopausal groups, the high BMI category was found to have a higher breast cancer incidence rate (Jung & Lee, 2009). The BMI results indicate a poor association with breast cancer risk. The average Namibian woman diagnosed with breast cancer is 28.40 ±5.819 standard deviation, overweight and obese. However, an observation demonstrated that 74% of the women diagnosed with breast cancer with a BMI ≥25 considered overweight appeared the most in age categories

40-65 years. These women were overweight and in the same class of the high-risk height category (1.59-1.62m).

Height: Many epidemiological studies have investigated the link between adult height and the risk of breast cancer in women. This study indicated that Namibian women with a height between 1.59 m to 1.62m are more likely to develop breast cancer than women with increasing height >1.67 and decreasing height <1.59 m. These findings align with other studies that suggest height association to breast cancer. Zhang et al., 2015 estimated that a 10cm increase in height was associated with a 17% raised risk of breast cancer. Adult height is a risk factor for breast cancer in women, and certain genetic variables and biochemical processes that impact adult height plays a vital role in breast cancer aetiology. Reports consider that adult height is the impacted is by caloric consumption and socioeconomic level during growth spurts and hereditary factors. Certain nutritional factors during childhood and adolescence have increased the risk of breast cancer. However, only a few studies have gathered enough extensive information on childhood and teenage nutrition and health status and pubertal development to conclusively separate the link of breast cancer risk with the adult height from these other factors. (Friedenreich, 2001; Mehta et al., 2001; Okasha et al., 2003; Zhang et al., 2015). As a result, it is unclear if height is simply a surrogate measure of early life exposures to breast cancer risk factors or whether height is causally connected to breast cancer risk in and of itself. It is also plausible that the link between height and breast cancer is causative, in which genetic and environmental variables influence height and, as a result, contribute to breast cancer risk via shared underlying biology (Zhang et al., 2015).

Menarche: While a woman's age at menarche does not always correspond to the commencement of breast growth, the two are strongly linked. Breast cancer is virtually unknown before menarche and exceedingly rare shortly after, making it nearly impossible to evaluate the short-term consequences of hormonal variations related with menarche by comparing breast cancer risk in women of similar ages before and immediately after menarche (Collaborative Group on Hormonal Factors in Breast Cancer, 2012). Early menarche is typically characterising as menarche occurring before 12, while some scholars define it as 10 or 11 years old. Furthermore, women who reach menarche before 12 have a 23% higher risk of breast cancer than those who begin menstruating at the age of 15 or later (Key, 2001). Women that have their menarche <12 years are generally considered early menarche. Women <12 are at high risk for several diseases, including breast cancer (Goldberg et al., 2020; N. Johnson et al., 2014) even so, the literature is primaeval. The

results for this study indicated that menarche was not associated with breast cancer as none of the women diagnosed with breast cancer had their menarche at <12 years for this study. The results for this study designated that only 1.5% of the sample population had their menarche <12 years, of which none were amongst the sample group diagnosed with breast cancer and 98. 5% had their menarche ≥12 years. The mean participants with breast cancer had their menarche at 14.9%, with a standard deviation of (1.86). Altogether, the average Namibian woman in the total sample size presented with late menarche of 14.74 years. The difference in results could be due to the difference in environmental, geographical and dietary factors.

Age at first pregnancy: Nulliparous women have a 20%–40% higher risk of postmenopausal breast cancer than parous women who have had their first child before the age of 25 (Rosner, 1996) (Pike, 2002) (Sweeney, 2004). Nulliparity is a known risk factor for breast cancer, especially when contrasted to parity at a young age (Schonfeld, 2011). Women who have not had a full-term pregnancy or who give birth beyond the age of 30 have a higher risk of breast cancer than women who give birth before 30. According to one study, breast cancer risk reduction from pregnancy does not begin until roughly 20 years after a woman's previous pregnancy (DePolo, 2019). Breast cancer has also been linked to a late age at first childbirth (> 30 years old) (Albrektsen, 2005). According to several studies, there is no link between age at first full term pregnancy and breast cancer risk (Aurin et al., 2020; Morrison et al., 1977; Warren Andersen et al., 2011). Other research suggests that having a first child at an older age may result in a lower outcome (Alsaker et al., 2011) or, to be more specific, breast cancer (Kroman et al., 1998; Rosenberg et al., 2004).

Menopause: The age at which a woman enters natural menopause varies greatly. Early menopause is thought to be a risk factor for osteoporosis and cardiovascular disease, while later menopause is thought to be a risk factor for breast cancer (Moron et al., 2009). The onset of menopause is not linked to an increased risk of cancer. Many cancers, including breast cancer, do, however, grow with age. Furthermore, several of the medications used to treat menopausal symptoms may increase or decrease a person's risk of cancer. Late menopause is usually considered after age 55 for breast cancer (Robinson, 2019). The results indicated that late menopause at ≥55 years was positively associated with breast cancer particularly for Namibian women, this result is in line with other studies. Menopause that comes late is mainly due to a hereditary predisposition. Because adipose tissue produces oestrogen, late menopause is typical among obese women, according to a research.

Hormone Replacement Therapy: For this study Hormone replacement therapy use was positively associated with breast cancer. In dissimilarity women with breast cancer used less HRT than the population of women without breast cancer. Generally, very few Namibian women are prone to use HRT at 4.5 % for the overall population of which 3.5% of women using HRT were not diagnosed with breast cancer. Grippingly the role of hormone replacement therapy (HRT) has been discussed for decades. HRT revealed significant benefits in early observational studies, more recently, randomized trials, such as the Women's Health Initiative (Chlebowski et al., 2015) which studied predominantly women several years after menopause began, found no such benefit and, in fact, an increased risk of breast cancer, leading to a sharp reduction in the use of HRT. Although HRT should predominantly consist of oestrogen, no specific HRT regimen may be recommended (Lobo, 2017). Each type of HRT seems to have a different effect on the risk of breast cancer even when administered for a short period of time, combination HRT increases the risk of breast cancer by roughly 75%. HRT that exclusively contains oestrogen raises the risk of breast cancer, but only if it is used for more than ten years (Denise Mann, 2021). To understand the effect that HRT use has on breast cancer further studies must be done regarding this over a longer period.

Family history: Although the influence of risk factors for breast cancer among women with a family history is not clearly characterized, it is an established risk factor for this disease and is used to identify women at higher risk(Colditz et al., 1996). The results for this study opposed the association of family history of breast and ovarian cancer as a risk factor for breast cancer, more so conflicting results have been reported regarding this result by other studies (Ahern et al., 2017; Brewer et al., 2017). However, studies have also indicated that family history of breast or ovarian cancer was not a risk factor for breast cancer(Román et al., 2017; Song et al., 2017). Regardless For high-risk women, a familial predisposition to breast cancer has a major impact on screening and follow-up recommendations. Family history can be in junction with other risk factors to determine the risk category of patients, but suggestively not as a single determinant for considering the risk association for Namibian women. for this study very, few Namibian women have generally a low recorded family history, this could be influenced by the lack of awareness from patients about breast cancer or family members not disclosing information regarding their diagnosis, this is an area then may be further investigated.

BIRADS Category: BI-RADS categories can be used for differentiation of malignant or benign breast lesions and calcifications in the breast(Hao et al., 2016; Mora-Encinas et al., 2015). In

their investigation, Michael et al and O Idowu et al discovered that radiologic-pathologic concordance was as high as 94.5% (Kumari et al., 2020). In this study radiologic-pathologic concordance was as high as 91.5%. BI-RADS classification should be considered as a risk factor as a reference for further investigations of the breast or follow-up annual mammograms.

5.2 Phase1; Tyrer Cuzick risk assessment evaluator

Doctors consider a Tyrer-Cuzick score of less than 15% to be at a medium risk of developing breast cancer. A breast cancer risk score of 15–19 % indicates a medium chance of developing the illness. Doctors typically consider a score of more than 20% to be high risk. They may suggest that persons in the high-risk group undergo additional annual screenings, such as a breast MRI (Johnson, 2021). Calculations that consider comprehensive family history must be made to determine who is at high risk. However, the results demonstrated an overall low lifetime risk of 6-10%, the most recorded percentage calculated, which amounted to 62% of the diagnosed population group. None of the women diagnosed with breast cancer had a lifetime risk calculation of 20%, although 5 % of the diagnosed group population fell between the 16-20% populations. The study suggests that the Tyrer Cuzick tool not be used solely to determine patients' risk; as indicated by the results of this study, it is not entirely compatible for Namibian women. Although the Tyrer Cuzick tool uses most of the established risk factors, these risk factors are not necessarily explicitly established for Namibian women as per the results of this study. Further research may exclusively investigate the Tyrer Cuzick tool's compatibility.

5.3 Phase 2; Breast cancer management and treatment

Invasive ductal carcinoma is the most common type of breast cancer(Breastcancer.org, 2019). This study indicated invasive ductal carcinoma as the most commonly diagnosed cancer at 43% amongst other breast cancer types; ductal carcinomas altogether were 65% of all breast cancer diagnoses. The most frequent kinds of breast cancer are treated with endocrine therapy. In hormone-sensitive tumours, endocrine agents work by blocking oestrogen's tumour-stimulating effects. A new generation of targeted medications works with endocrine agents to help patients with metastatic disease live longer. Endocrine medication is frequently sustained for years, and long-term survival is typical, while toxicities are widespread due to changes in oestrogen's physiologic effects. As a result, primary care

professionals must stay informed about their patients' requirements during and after treatment (Johnston, 2015). One of the most common types of cancers is breast cancer, and early diagnosis is essential in its treatment (Ak, 2020). Currently most of the options required to treat breast cancer are provided for patients, although the resources are limited. Surgery, chemotherapy, radiotherapy and targeted therapy are commonly used in Namibia to treat breast cancer. Immunotherapy was not available option at the AB May oncology and gene testing center. The results also indicated a need for screening modalities such as mammograms at the state level due to patients arriving with advanced disease for treatment. Physicians who specialise in diverse fields of cancer management, such as surgery, radiation oncology, and medical oncology, work together with radiologists and pathologists to improve a patient's complete treatment plan, which may include a diversity of treatments (American Society of Clinical Oncology, 2021). A multidisciplinary team is what this is referred to as. The results indicated multidisciplinary events organised and taking place, but the presence of all necessary parties for the event was not established in this study. The results also confirmed the implementation of survivorship plans and groups as part of breast cancer management. In addition, a holistic, integrated health system for breast cancer management is encouraged for a smooth transition of the patient from diagnosis to treatment.

CHAPTER SIX

CONCLUSION

This chapter will settle the study by summarising the crucial research outcomes in relation to the research aims and research questions, as well as the value and impact thereof. It will also criticise the limitations of the study and suggest recommendation for future research.

6.1 Summary of findings

This study aimed to assess the most common risk factors of breast cancer such as Age, Weight, Height, BMI, Menarche, Age at 1st pregnancy, Parity, Menopause, HRT use, Family history of breast and ovarian cancer and BIRADS category amongst Namibian women visiting the Medical Imaging departments. To further determine the breast cancer pre-screening tool used, to consider the risk factors assessed as compatible for Namibian women. Finally, to assess how management and treatment procedures of breast cancer are linked to the breast disease outcomes.

The results indicated that some of the intrinsic and extrinsic breast cancer risk factors are not so common amongst Namibian women like Weight, BMI, Menarche, Age at first pregnancy, Menopause, Family History and HRT used. However, common risk factors are participants Age, Height and BIRADS specific to Namibian women can be suggested. Namibian women between the ages of 40 to 65 are generally a high risk, although this is encouraging since that age group of women are receptive for breast screening. Women between 162 to 159 cm are point out to be at high risk for breast cancer specific to Namibian women. In this study BIRADS category results shown to be the most accurate risk factor for determining breast cancer risk. Most women with a BIRADS 4 or 5 were presented with breast cancer. BIRADS risk factor also indicated to be the most common risk factor that can be used to accurately determine the patient's risk for breast cancer, however this risk factor can only be used after a mammogram is performed and further be used as a baseline risk factor for follow-up breast investigations or screening.

Results further indicated that the Tyrer Cuzick screening tool for breast cancer was not compatible for the Namibian women. Women diagnosed with breast cancer fell into the low risk category when the pre-screening risk assessment tool was used to calculate the Namibian women life-time risk. Screening tool's impact on the efficiency with which health care workers triage patients to cancer genetics services is needed in primary care settings.

The results confirmed that there are no known genetic testing facilities in Namibia. This puts Namibian women at a disadvantage even if they knew their risk for breast cancer in accordance to a reliable breast cancer risk assessment tool.

Finally, the most commonly diagnosed breast cancer type as indicated by the results is invasive ductal carcinoma. Even so, Namibian women have a variety of options readily available for breast cancer treatment. However, the facilities shown strain as a lack of pre-screening, screening, a lack of knowledge, and inadequate resources to be the key hurdles in combating the breast cancer burden in Namibia. Although there are screening facilities provided in the private sector such as Medical Imaging and others, there is not enough screening or active facilities for breast screening in the state to accommodate patients without medical insurance, even though, advanced cases are usually referred from state to private institutions for screening. Erecting increased screening infrastructure and facilities could save lives. Although there is knowledge about the management of cancer, there is very little effort to combat the situation, several characteristics such as the scarcity of constantly available screening facilities such as mammograms, insufficient access to medications and a scarcity of oncology professionals.

6.2 Significance of the study

This study supports to be a part of very little baseline studies for breast cancer research in Namibia to encourage researchers to continue the journey of improving the fight for breast cancer. The research may help in revaluating the policies and protocols in place for risk assessment for breast cancer in Namibia. This study may unfold the value of breast cancer risk assessment, as it is critical for determining whether women will profit from more intense breast cancer observation. Risk assessment and identification of high-risk women may allow for referral to health-care providers who specialize in cancer genetics counselling and testing for breast cancer-related germline mutations (e.g., BRCA), patient counselling on risk-reduction possibilities, and cascade testing to classify family members who may also be at risk.

6.3 Limitations

Precise incidence numbers were difficult to come by due to incomplete data on risk forms, context of data with patients avoiding answering some personal question due to sensitivity

of data, unclear data filing, lack of quality assurance for correct data filing and finally economic and IT restrictions as there are still manual paper filing systems used as compared to the electronic systems used. There is a breast cancer incidence variability from national population-based data due to methodology, lack of health service access, lack of pathologic diagnosis and true differences in risk factors.

The study was altered to mixed method of prospective and retrospective to accommodate the amount of data needed. The information available was then used to its maximum potential. Patients, oncologist, medical institutions seemed sceptical to take part in the research for a variety of reasons, even when confidentiality was assured. This indicated the lack of knowledge on the importance of research regarding combating a disease amongst already mentioned data challenges.

There were challenges to retrieve data or use data from some medical institution regarding breast cancer, even when the Namibian Ministry of Health and Namibian University of Science and technology have measures in place to secure confidentiality and security.

6.4 Recommendations

Future researchers can perhaps embark on engaging the community before implementing their studies, however, they would need the institutions where data can be collected on board to embark on the journey with them.

Policy makers should perhaps invest in encouraging research in the relative country rather than depending on research from policy makers as well to adapt policy specifically related to the population at interest.

This research encourages the need for other imaging departments around Namibia to prospectively collect patient data and implement adequate information technologies (IT) and data processing resources. These data must be made available for proper epidemiological studies in the National Cancer Registry database. As for the oncology centre this research encourages a proper integrated system and guidelines from the beginning of the assessment of Breast cancer to the treatment and or maintenance of the disease at a holistic level.

Large-scale mammography in the defined age categories may result in a decline in breast cancer-related mortality. Women at average risk of breast cancer should be presented screening mammography starting at age 40 years not only at the private institutions, but

also in the state institutions. Patients Risk assessment history must be regarded and treated as important and so be documented properly on a large scale with policies and institutions in place to keep records accountably and not on a seasonal basis. Although the mentioned common risk factors amongst Namibian women can be used as an emphasis during pre-screening for breast cancer this risk factors need further detailed research. Even though the risk of discovery in categories suggestive of malignancy has dropped at the national level, certain states need to strengthen the use of mammography-based breast cancer screening programs and expand the target population's involvement(Navarro-Ruíz & Reyna-Sevilla, 2021).

Breast cancer lesions may be overlooked on mammography due to dense tissue masking, according to the Boyd and BIRADS classification systems. As a result, patients with a high BIRADS or Boyd score should be evaluated further(Meggiorini et al., 2016). Primary care physicians would profit from devising procedures, in collaboration with their collaborating radiologists, to ensure that all women who require additional imaging (BI-RADS codes 0 and 3) and those who have worrisome mammograms (BI-RADS codes 4 and 5) receive adequate follow-up. This could include the formation of an office register to ensure proper management, as well as the informative and emotional assistance that is required. Furthermore, BIRADS categories can be used confidently for breast cancer screening risk assessment purposes.

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Appendices:

Appendix A: Certificate; permission for research from Ministry of Health and Social Services

0813267321 / 0814795 IC

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198 | Ministerial Building | Tel: 061 – 203 2507
Windhoek | Harvey Street | Fax: 061 – 222558
Namibia | Windhoek | E-mail: hashipu87@gmail.com

OFFICE OF THE EXECUTIVE DIRECTOR

Ref: 17/3/3 MSK
Enquiries: Mr. A. Shipanga

Date: 17 December 2019

Ms. Martinlina S. Karutjaivn
PO Box 87321
Eros
Windhoek

Dear Ms. Karutjaiva

Re: Breast cancer associated risk factors and management among women attending Medical Imaging departments' in Namibia.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. **Kindly be informed that permission to conduct the study has been granted under the following conditions:**

3.1 The data to be collected must only be used for academic purpose;

3.2 No other data should be collected other than the data stated in the proposal;

3.3 Stipulated ethical considerations in the protocol related to the protection of Human Subjects should be observed and adhered to, any violation thereof will lead to termination of the study at any stage;

3.4 A quarterly report to be submitted to the Ministry's Research Unit;

3.5 Preliminary findings to be submitted upon completion of the study;

3.6 Final report to be submitted upon completion of the study;

3.7 Separate permission should be sought from the Ministry for the publication of the findings.

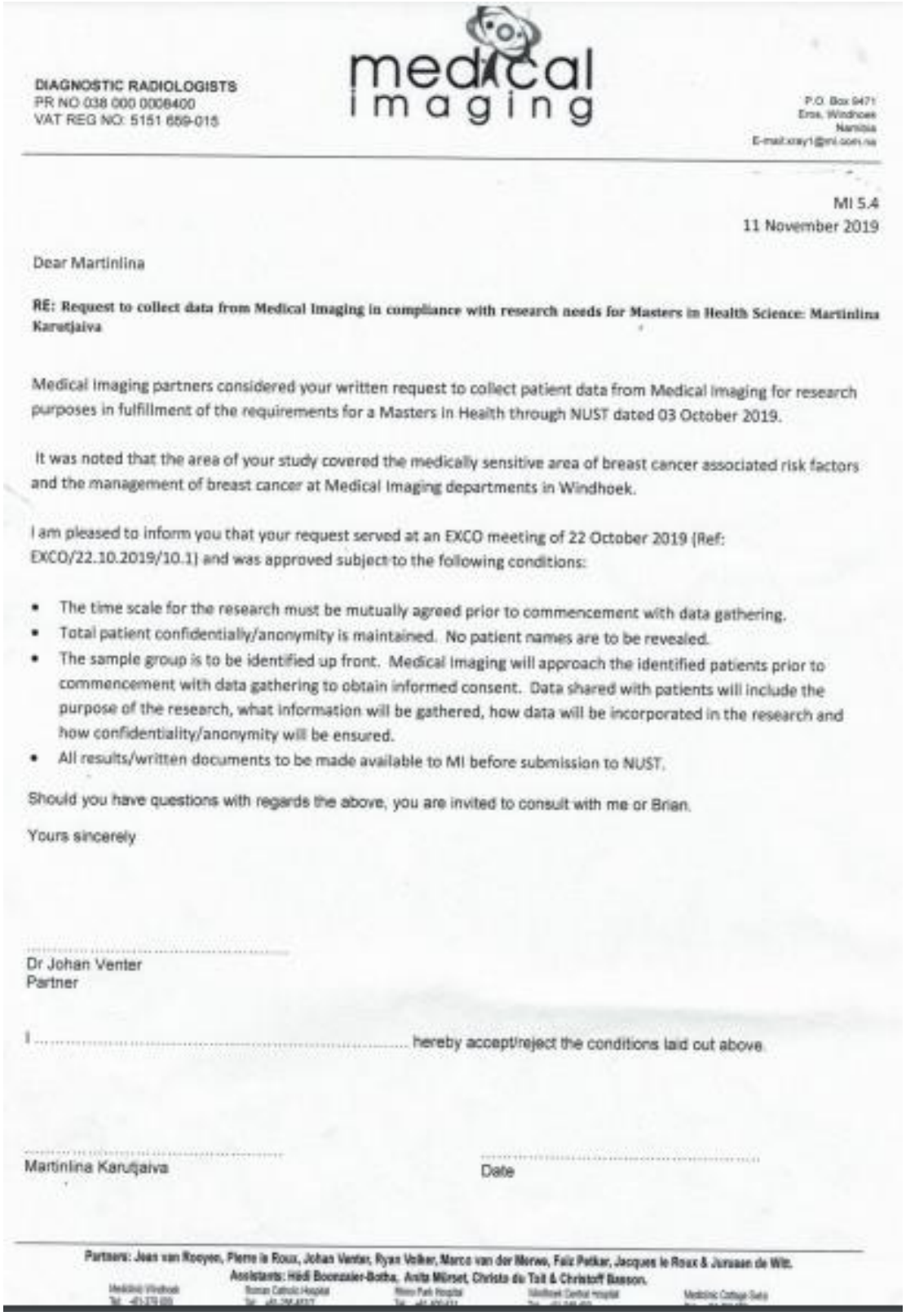
4. All the cost implications that will result from this study will be the responsibility of the applicant and **not** of the MoHSS.

Yours sincerely,

BEN NANGOMBE
EXECUTIVE DIRECTOR

"Health for All"

Appendix B: Permission from Medical Imaging



DIAGNOSTIC RADIOLOGISTS
PR NO 038 000 0006400
VAT REG NO: 5151 659-015

medical imaging

P.O. Box 9471
Eros, Windhoek
Namibia
E-mail:xray1@mi.com.na

MI 5.4
11 November 2019

Dear Martinlina

RE: Request to collect data from Medical Imaging in compliance with research needs for Masters in Health Science: Martinlina Karutjaiva

Medical Imaging partners considered your written request to collect patient data from Medical Imaging for research purposes in fulfillment of the requirements for a Masters in Health through NUST dated 03 October 2019.

It was noted that the area of your study covered the medically sensitive area of breast cancer associated risk factors and the management of breast cancer at Medical Imaging departments in Windhoek.

I am pleased to inform you that your request served at an EXCO meeting of 22 October 2019 (Ref: EXCO/22.10.2019/10.1) and was approved subject to the following conditions:

- The time scale for the research must be mutually agreed prior to commencement with data gathering.
- Total patient confidentially/anonymity is maintained. No patient names are to be revealed.
- The sample group is to be identified up front. Medical Imaging will approach the identified patients prior to commencement with data gathering to obtain informed consent. Data shared with patients will include the purpose of the research, what information will be gathered, how data will be incorporated in the research and how confidentiality/anonymity will be ensured.
- All results/written documents to be made available to MI before submission to NUST.

Should you have questions with regards the above, you are invited to consult with me or Brian.

Yours sincerely

.....
Dr Johan Venter
Partner

I ..... hereby accept/reject the conditions laid out above

.....
Martinlina Karutjaiva

.....
Date

Partners: Jean van Rooyen, Pierre le Roux, Johan Venter, Ryan Volker, Marco van der Merwe, Faiz Petkar, Jacques le Roux & Juraan de Witt.
Assistants: Heidi Boonzaier-Botha, Anita Mirset, Christo du Toit & Christoff Basson.

Appendix C: Permission from Office of the Chief Medical Superintendent Windhoek Central Hospital

Private Bag 13215
Windhoek
Namibia
Enquiries: Ms. S.Iipinge Ref. 17/3 / 3

Harvey Street
Windhoek Central Hospital

Tel. No: (061) 203 3024
Fax No: (061) 222886

Date: 11 February 2021

OFFICE OF THE CHIEF MEDICAL SUPERINTENDENT

Mr. Martinlina Karutjaiva
0818369323

Dear Mr.Karutjaiva

SUBJECT: PERMISSION TO COLLECT DATA ON THE ASSESSMENT OF THE MOST COMMON BREAST CANCER RISK FACTORS AMONG NAMIBIAN WOMEN AT MEDICAL ONCOLOGY AND RADIOLOGY, WINDHOEK CENTRAL HOSPITAL

1. Reference is made to your application to conduct the above-mentioned study.
2. This letter serves to inform you that permission has been granted for you to do research on the above mentioned subject as you have requested and does not include any remuneration.
3. Patient/Client's information should be kept confidential at all times.
4. Preliminary findings copy to be submitted to Customer care office, Windhoek Central Hospital upon completion of the study.

Thank you.

Yours sincerely,

DR.F.ZAM
ACTING CHIEF MEDICAL SUPERINTENDENT

MINISTRY OF HEALTH AND SOCIAL SERVICES
Private Bag 13215
11 -02- 2021
Windhoek Namibia
WINDHOEK CENTRAL HOSPITAL

Appendix D: Phase 1 Patient consent and Risk assessment questionnaire

0155R

Informed Consent to Participate in Research Study

Name of Institution: Namibian University of Science and Technology

Department: Masters of Health Sciences

Title of Research Project: Assessment of Breast Cancer Associated Risk Factors among women attending Medical Imaging in Windhoek Namibia.

Name of Principal Investigator: Martinlina Seranline Karutjaiva

Phone Number of Principal Investigator: 0818369323

Location of Researcher: Roman Catholic hospital

Approval of research from Ministry of Health was granted, certificate obtained.

PURPOSE AND BACKGROUND

Martinlina Seranline Karutjaiva a registered mammographer at Medical Imaging is conducting research on the assessment of Breast Cancer Associated Risk Factors among women attending Medical Imaging in Windhoek Namibia.

The purpose of your participation in this research is to help theresearcher to assess the common risk factors of breast cancer. Medical Imaging currently uses an international breast cancer risk assessment tool called the Tyrer Cuzick or IBIS tool.The Tyrer-Cuzick model, or IBIS tool, is used to calculate a person's likelihood of carrying the BRCA1 or BRCA2 mutations. It estimates the likelihood of a woman developing breast cancer in 10 years and over the course of her lifetime. The tool is used to help inform a person's decision-making about genetic counseling and testing. If the model predicts a 10% or greater chance that the woman has a mutation in BRCA1, BRCA2, or both, genetic counseling is advised.

The researcher is doing this study to identify if the IBIS Risk factor calculation tool is actually applicable for Namibian women.

You are selected to participate in this research because your involvement in this research will provide information that will be used to create a specific reference range for breast cancer for Namibian women.

PROCEDURES

If you agree to participate in this research study, the following will occur:

You will fill in a specially designed breast cancer risk assessment form/questionnaire prior to your routine breast examination or follow-up exam. Your identity will be kept confidential at all times, instead of using your name; a code will be used for identity purposes. Your diagnostic report will be used for comparing the outcome of your risk calculated on the Tyrer Cuzick Model. If you are to get a biopsy the outcome of your results will also be compared with the Tyrer Cuzick risk percentage. This will help the researcher identify a specific estimated population's risk percentage.

RISKS

No risk towards the Participant, due to professional confidentiality and anonymity.

VOLUNTARY PARTICIPATION

Your decision whether or not to participate in this study is voluntary and will not affect your relationship with the University of Science And Technology or Medical Imaging. If you choose to participate in this study, you can withdraw your consent and discontinue participation at any time without prejudice.

QUESTIONS

If you have any questions about the study, please contact Martinlina Karutjaiva by calling 0818369323 you can also contact Dr Aboua Yapo by calling 0816989127 with any questions about the rights of research participants or research related concerns. Participants are most welcome to receive information on the outcome of the study by contacting the researcher. **Please note** that this information can only be communicated once the project is done.

CONSENT

YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN A RESEARCH STUDY. YOUR SIGNATURE BELOW INDICATES THAT YOU HAVE DECIDED TO PARTICIPATE IN THE STUDY AFTER READING ALL OF THE INFORMATION ABOVE AND YOU UNDERSTAND THE INFORMATION IN THIS FORM, HAVE HAD ANY QUESTIONS ANSWERED AND HAVE RECEIVED A COPY OF THIS FORM FOR YOU TO KEEP.

Signature _____ Date _____ Research Participant

Signature _____ Date _____

Martinlina Karutjaiva Cell: 0818369323

NAMIBIA UNIVERSITY OF SCIENCE AND TECHNOLOGY

RISK ASSESMENT QUESTIONAIRE

Participant code Number:	Date of birth:
Did you participate this year? (If you participated already please sign and date form thank you)	Yes No
Reason for mammogram	Routine symptomatic
Have you had genetic testing done?	
Do you know the risk of breast cancer?	Yes No
Are you Namibian or lived 10 years in Namibia?	Yes No
Have you ever been diagnosed with ductal carcinoma in situ (DCIS)?	Yes No
Have you ever been diagnosed with lobular invasive carcinoma in situ (LCIS)?	Yes No
Have you ever been diagnosed with ovarian cancer?	Yes No
Have you had a hysterectomy?	Yes No
Menopause?	Yes No Maybe
How old are you?	
What is your height?	
What is your weight?	
What is your breast size? If unsure please ask mammographer to help you.	
Have you had breast surgery before? If yes please specify.	
Are you on hormone replacement therapy? If yes please specify and how long you have used HRT.	
Are you on any contraceptives? If yes please specify.	
At what age did you start your menstrual cycle?	
At what age did you have your first child?	
How many full term pregnancies have you had?	
What was the longest time you have breast fed?	
Have you had any miscarriage? Please state amount if so	
What region are you from currently?	
What is your race?	black / white / mixed / unknown
What is your ethnicity? (Please tick appropriate box)	Ovambo / Herero / Damara / Nama / San Kavango / Himba / Mixed / Tswana / Caprivian Oorlam / Ikung / Afrikaner / German / British Portuguese / Unknown / other
How many of your sisters, daughters, or mother	

have had breast cancer?			
Have you ever had a breast biopsy/ FNA?	Yes ◯	No ◯	Maybe ◯
If yes results, BREAST CANCER	Yes ◯	No ◯	Maybe ◯
Have you had your chest radiated before?	Yes ◯	No ◯	Maybe ◯

Breast Cancer Family History

1ST Degree family

Self	Mother	Sisters	Daughters
Ovarian Cancer			
Breast Cancer			
Age at Diagnosis			
One/ bothsides			

2nd Degree family

	Fathers mother	Mothers mother	Fathers sister	Mothers sister	Grand daughters	Brother /sister daughter
Ovarian Cancer						
Breast Cancer						
Age at Diagnosis						
One/ bothsides						

3rd Degree family

	Cousin	Great- grand parent	Great Aunt
Ovarian Cancer			
Breast Cancer			
Age at Diagnosis			
One/ bothsides			

Appendix E: Phase 2, oncologist and questionnaire

TITLE OF STUDY

Breast cancer-associated risk factors and management among women attending Medical Imaging departments' in Namibia.

PRINCIPAL INVESTIGATOR

Martinlina Karutjaiva

Senior Radiographer at Medical Imaging

Master of Health Sciences

Faculty of Applied Health Sciences

Tel: 0818369323

seranline@gmail.com

PURPOSE OF STUDY

You are being asked to take part in a research study. Before you decide to participate in this study, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully. Please ask the researcher if there is anything that is not clear or if you need more information.

The **purpose** of this study is to understand the risk factors that supposedly contribute to the cause of breast cancer and to determine which the most common risk factors amongst Namibian women are to create a reference range specifically for Namibian women. One of the aims of this researcher is to create awareness regarding the importance of risk factors and the assessment of these factors. This may help contribute vastly in Breast cancer treatment and prevention approaches.

RISKS

Your information will always be kept confidential and anonymous according to the Ministry of Health, NUST and Medical Imaging guidelines. Patient confidentiality is always of utmost importance.

Please Note: You may decline to answer any or all questions and you may terminate your involvement at any time if you choose.

BENEFITS

- This study's goal is to help educate women about their breast cancer risk and raise awareness about risk-appropriate breast cancer screening and prevention methods. Since breast cancer is such a common disease, focusing primary prevention efforts on high-risk women could have a significant public health effect.
- This research will help us determine the efficiency of risk assessment tools used to determine the risk for breast cancer.
- If we know what percentage of women in Namibia are generally a “high risk” for breast cancer and may be candidates for anti-oestrogen pills to reduce their risk of breast cancer, also known as “chemoprevention.” Many women and their primary care partners, on the other hand, are unaware of their high-risk status or the treatment options for breast cancer.
- This research may contribute to the treatment approaches for breast cancer specific to Namibian women.

CONFIDENTIALITY

Your responses to this survey will be anonymous. Please do not write any identifying information on your survey. Every effort will be made by the researcher to preserve your confidentiality including the following:

State measures taken to ensure confidentiality, such as those listed below:

- Assigning code names/numbers for participants that will be used on all research notes and documents

- Keeping notes, interview transcriptions, and any other identifying participant information in a locked file cabinet in the personal possession of the researcher.

Participant data will be kept confidential except in cases where the researcher is legally obligated to report specific incidents.

CONTACT INFORMATION

If you have questions at any time about this study, or you experience adverse effects because of participating in this study, you may contact the researcher whose contact information is provided on the first page. If you have questions regarding your rights as a research participant, or if problems arise which you do not feel you can discuss with the Primary Investigator, please contact the NUST Masters and Doctorates coordinator directly DR Aboua Yapo tell: 061 207-9111

VOLUNTARY PARTICIPATION

Your participation in this study is voluntary. It is up to you to decide whether to take part in this study. If you decide to take part in this study, you will be asked to sign a consent form. After you sign the consent form, you are still free to withdraw at any time and without giving a reason. Withdrawing from this study will not affect the relationship you have, if any, with the researcher. If you withdraw from the study before data collection is completed, your data will be returned to you or destroyed.

CONSENT

I have read and understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study.

Participant's signature _____ Date _____

Investigator's signature _____ Date _____

Please kindly answer the following questions:

1. Is there a treatment policy or guideline available for breast cancer in your department? **YES/NO**
2. Is there an option to do BRCA1 & BRCA 2 gene testing in your department? **YES/NO**
3. Would you recommend genome testing? **YES/NO**
4. Do you have a treatment policy in place for recurrent breast cancer? **YES/NO**
5. Do you know of any facilities in Namibia where gene testing for breast cancer can be done? **YES/NO**
6. Are there chemoprevention options available for Namibian women? **YES/NO**
7. Do patients understand their treatments options for breast cancer? Scale from 1 to 10. _____
8. Do you think that there are enough breast cancer treatment options for Namibian women? YES/NO
9. What is the most common method used to treat breast cancer in your department?
    a. Surgery
    b. Radiation therapy

a. Hormone therapy
b. Target therapy
c. Chemotherapy
d. other

1. What are the available treatment options for women diagnosed with breast cancer in your department?
    a. Surgery
    b. Radiation therapy
    c. Hormone therapy
    d. Target therapy
    e. Chemotherapy
    f. other
2. What challenges are oncologists facing regarding breast cancer treatment approaches in the Namibian setting?
    a. Lack of proper facilities
    b. Intense work load
    c. Lack of enough digital facilities
    d. Patients not returning for follow-up treatment
    e. Patients not understanding treatment options
    f. Patients showing up on time for treatment
    g. Patients showing up for treatment with advanced breast disease
    h. Running out of resources
    i. Cooperation from referral doctors
    j. Other
    k. No of the above
3. On a scale of 1 to 10 do most women present with advanced breast cancer when they get to oncology?
4. Are you currently using digital or manual methods for patient information and records?
    a. Digital
    b. Manual
5. What would you recommend be done to improve on the already available treatment approaches?
    a. Increase resources for treatment
    b. Educate and create awareness on breast cancer at large

a. Incorporate digital facilities
b. Create a holistic integrated system
c. Incorporate digital filing system at large
d. Employ more oncology health workers
e. Employ more oncologist
f. Increase facilities

1. On a scale of 1 to 10 do patients show for standing follow-up treatments for breast cancer? _____
2. On a scale of 1 to 10 do patients follow the recommended regimens for breast cancer treatment? _____
3. Is knowing patients breast cancer risk factors important?
4. Should patients' risk be recorded and filed?
5. Do you incorporate survivorship care plans during visitations?
   a. Yes
   b. No
   c. never
6. Do you share information with patients' surgeons?
   a. Yes
   b. No
   c. Never
7. Is good supportive care associated with survival advantages amongst Namibian women?
8. Do you track patients for recall/follow-up?
   a. Yes
   b. No
   c. sometimes
   d. never

THANK YOU FOR YOUR TIME IN ANSWERING THESE QUESTIONS!!